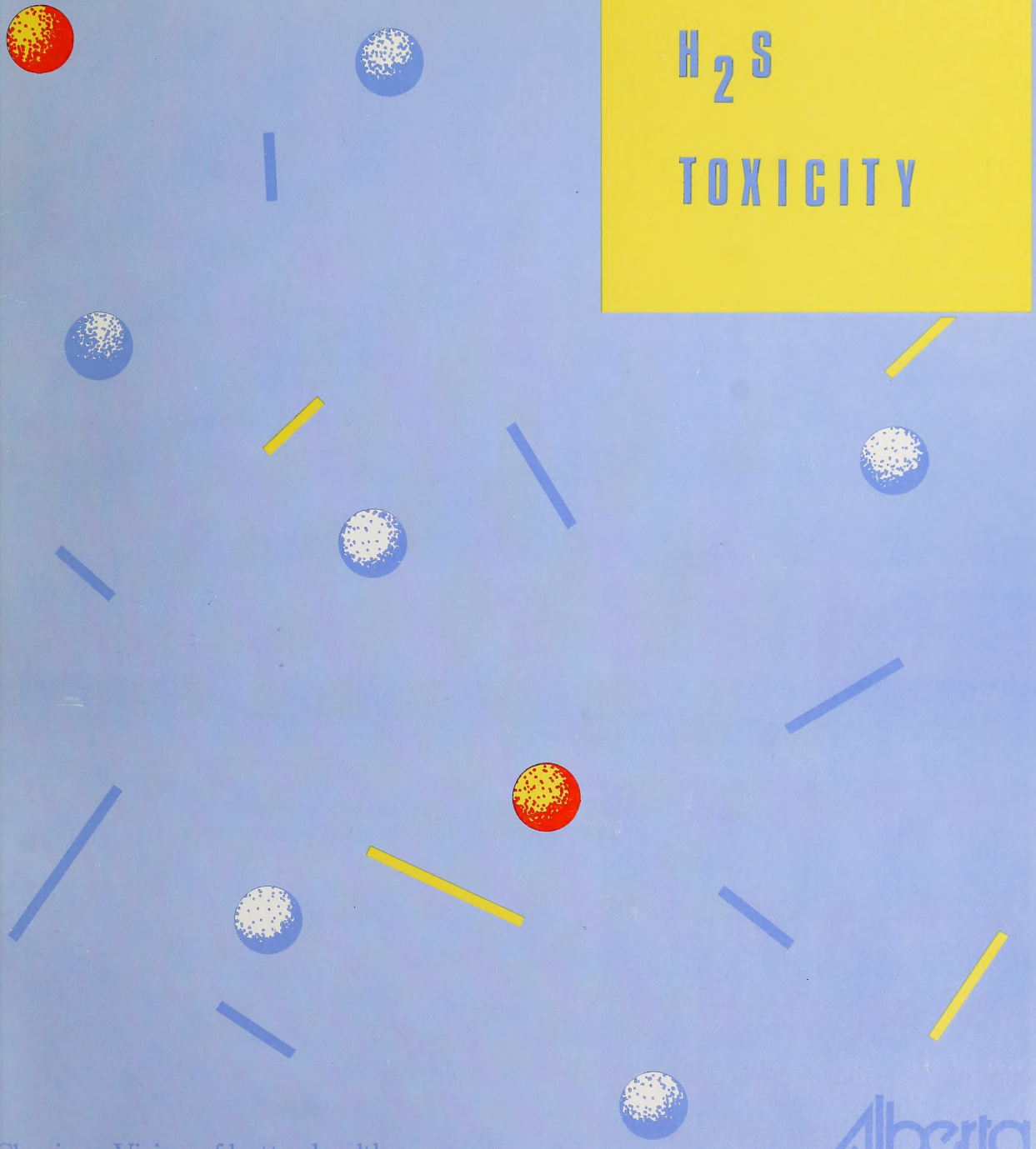
# REPORT ON $H_2S$ TOXICITY



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In Replying Please Quote:

August 29, 1988

Mr. Jan Skirrow
Deputy Minister
Alberta Community and Occupational Health
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Dear Mr. Skirrow:

I have the pleasure to transmit to you this report entitled REPORT ON $H_2S$ TOXICITY, which was prepared by the Ad Hoc Committee on $H_2S$ Toxicity. The Committee, with representatives from the petroleum industry, academic institutions, and government agencies, was established by the Department to document the known health effects of short-term exposure to hydrogen sulfide gas. The purpose of the research was to assist the Department in establishing evacuation guidelines in the event of an uncontrolled release of $H_2S$.

The information compiled by the Committee represents the most current knowledge on this topic. Evacuation guidelines can now be established, based on the scientific criteria contained in the report. The Department is indebted to the members of the Committee for their efforts in compiling and publishing this document.

Yours sincerely,

Dennis Barr
Acting Assistant Deputy Minister
Public Health Division

enclosure



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# Acknowledgements

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The committee also wishes to express its sincere appreciation to Mr. David Gibson and Mr. Maurice Taylor (Alberta Occupational Health and Safety Division) and Mr. Al Schulz (Alberta Environment) for their valuable review and comments on the initial drafts.

Finally, the committee wishes to recognize the extensive efforts and patience of Mr. Ed Collom (Alberta Health) in reviewing, editing and submitting the final version of this document for publication.

# Executive Summary

In October, 1982 a sour gas well being drilled near Lodgepole, Alberta blew out of control. For the next 67 days specialists fought to regain control of the well. As a result of this event and high public concern over the health risks associated with exposure to sour gas, the Energy Resources Conservation Board conducted an extensive inquiry into what happened, why it happened and how it might be avoided in the future.

One of the recommendations arising from the Lodgepole Inquiry was the need for stricter exposure standards for those persons judged to be more susceptible to hydrogen sulphide ($H_2S$). As a result, a recommendation was forwarded to the then existing Provincial Board of Health for further consideration of this particular issue. In 1985 a committee was formed within Alberta Social Services and Community Health (SSCH) to complete this task. There was no industry representation on this committee.

In 1986, as a result of industry concerns, a new Ad Hoc Committee on $H_2S$ with representatives from industry was struck to review the evacuation levels previously proposed by SSCH and the scientific rationale for each.

The specific terms of reference for the committee were:

1. To assess the scientific evidence for low level acute, subacute and chronic effects of $H_2S$ on humans in the range 0 to 100 ppm, and especially the 0 to 20 ppm range.
2. To clarify the issue of the effects of low levels of $H_2S$ on sensitive individuals.

The committee was asked to submit its final report to Alberta Community and Occupational Health, who would use it to develop evacuation guidelines for Albertans during uncontrolled sour gas releases.

The committee undertook an extensive literature review and, where possible, obtained original articles, abstracts and review papers. Definitive data from well-designed studies were weighed against more anecdotal observations in the search for good end points from which conclusions could be drawn. The review included a comparison of animal research data, human experimental data and human epidemiological studies.

In conducting its critical assessment, the committee relied heavily on its collective technical knowledge of the health effects of $H_2S$, as well as its professional judgment in areas where the scientific literature was not as strong as would be preferred.

As the committee initiated its review, it became increasingly clear that scientific terminology and concepts varied considerably from one discipline to another. In an attempt to minimize confusion for the reader yet to maintain scientific integrity in the discussion of various terms and concepts, the committee felt it worthwhile to provide some basic background. This is presented in Section II.

Based on the analysis of the scientific literature, it seems clear that some individuals may be more susceptible to the effect of $H_2S$ than others. Other factors besides dose and duration of exposure may in part account for hypersusceptibility of a small proportion of the population to $H_2S$ at low levels of exposure at any given time. These include:

a. mixed exposure with other chemicals at the same time (e.g. $CS_2$, CO, $CO_2$, $SO_2$, $O_3$, $NO_x$, $NH_3$, mercaptans or particulates) and/or recent exposure to chemicals in other settings (e.g. home, garden, work).
b. pre-exposure to medications, alcohol and/or other drugs.
c. pre-existing and/or current diseases, physiological conditions (e.g. nutritional/hormonal status), psychological status, and cardiovascular impairment.

While the committee recognizes that the following do not represent all possible situations where hypersusceptibility may exist, categories of individuals who may be expected to show increased susceptibility to $H_2S$ exposure include:

a. individuals with eye or respiratory tract problems — local irritant effects of $H_2S$ could aggravate pre-existing conditions (e.g. conjunctivitis, eye infection, tuberculosis, viral pneumonia, asthma, emphysema, bronchitis).
b. individuals with severe anemia — certain data indicate that detoxification of $H_2S$ requires the presence of adequate levels of oxygen in the blood.
c. individuals with lowered resistance to bacterial infections (e.g. immunosuppressed patients).

The committee concludes the following from its review:

1. $H_2S$ by itself is a broad spectrum toxicant that can elicit numerous psychological and

biological responses in the 0 to 20 ppm range with which this review was concerned. As with any chemical all organ systems respond variably to different levels of $H_2S$ with no given level affecting all systems equally at the same time or rate.

2. In general, single or repeated exposures of "normal, healthy adults" to $H_2S$ in the 0 to 5 ppm range have not resulted in clinically-detectable irreversible biological or psychological effects. Whether this is true for hypersusceptible individuals is not currently known. This areas needs further research.
3. Although reversible adverse effects may result in temporary discomfort or changes in organ function, they have not been found to have a lasting impact to date.
4. There are certain factors that may increase susceptibility of humans to $H_2S$ for which the scientific evidence is not strong. These include the use of alcohol (Poda, 1966; Beck and Donini, 1979); age, as in the case of the very young, the elderly or infirmed; and pre-existing cardiovascular disease (USPHS 1964).
5. There remains a lack of good scientific data about the long-term, low level chronic effects on community populations and on the work force in sour gas operations.

NOTE:
During the preparation of this report the department has gone through various name changes — from Social Services and Community Health, to Community and Occupational Health, and in September, 1988, Alberta Health was established.

# Background

In October, 1982, a sour gas well being drilled near Lodgepole, Alberta, blew out of control. For the next sixty-seven days specialists fought to regain control over the well. During this period two specialists lost their lives and numerous people residing near and far removed from the blowout site complained of health effects and feared for their safety.

Public concern was intensified by heavy media coverage, unresolved health concerns in southwest Alberta where two major sour gas facilities were operating, and memories of a similar incident in 1977 in the same area. As a result of this, a full public inquiry was announced in January, 1983, to examine in detail what happened, why it happened, and how it might be avoided in the future.

Of particular interest to the inquiry panel, headed by the Energy Resources Conservation Board (ERCB), were two health-related questions:

1. Are sour gas emissions a hazard to human health?
2. Are the responses to the emergency following the blowout adequate to minimize the effect on human health?

The answers to these questions were particularly important in assessing government and industry response to the blowout, especially public safety measures that were instituted. It is here where evacuation standards played a major role.

Given the public concern over the known toxicity of $H_2S$, the major toxic component of sour gas, a decision was made by Government public health authorities during the blowout period to use evacuation standards derived from the Alberta occupational exposure limit (OEL) of 10 ppm for 8 hours. This created considerable confusion in the minds of the public over what limits were in effect and how these had been established since the evacuation limits were not the same as the OEL. The inquiry panel concluded that the following limits were in place during the blowout:

1. Residents to consider evacuation if $H_2S$ concentrations become 5 ppm for 6 hours or 10 ppm for 1 hour.
2. Residents urged to evacuate at 15 ppm if an increasing trend exists.
3. Mandatory evacuation of all residents at 20 ppm for any period of time.

However, considerable confusion and uncertainty also existed over the evacuation standard being used for so-called "sensitive individuals." Although evidence presented to the inquiry implied that 5 ppm for 6 hours or 10 ppm for 1 hour was also intended to protect "sensitives," members of the public criticized the government agencies for not clarifying how this standard had been developed and what groups in the population were considered sensitive.

To address these concerns, Alberta Social Services and Community Health formed a committee in 1985 to review existing guidelines for action for sour gas, the literature supporting these guidelines, and the range of health in the normal population. No industry input was involved. The committee concluded the following:

1. The standards should focus on short term health effects.
2. There should be two basic standards:
   a. ≥1 ppm for sensitive individuals
   b. ≥20 ppm for mandatory evacuation
3. Standard sub-levels should be incorporated so that individuals would be advised of what is happening between 1 to 20 ppm. For example:

| | | |
|---|---|---|
| 1.0 ppm | = | voluntary evacuation for sensitive individuals with pre-existing health problems (who experience problems) |
| 5.0 ppm | = | voluntary evacuation for individuals without pre-existing health problems (who are experiencing increasing difficulty) |
| 10.0 ppm | = | occupational exposure limit |
| 15.0 ppm | = | levels beginning to critically approach 20.0 ppm |
| 20.0 ppm | = | urgent mandatory evacuation |

4. Sensitive individuals include pregnant women, children — especially pre-schoolers, patients being treated with immune suppressants, as well as people with pre-existing health problems such as:
   a. chronic respiratory disorders (e.g. bronchial asthma, bronchitis, emphysema)
   b. acute respiratory infections
   c. chronic cardiac failure
   d. hepatic disease
   e. neurological problems
   f. eye problems

These conclusions and criteria were incorporated into the Government of Alberta's Emergency Response Plan for a Sour Gas Release (Alberta Public Safety Services, 1986), and the ERCB's Evacuation and Ignition Policy. The latter have been used as standards in delineating emergency planning zones by companies making application to the ERCB to drill sour gas wells.

These guidelines created concern within the oil and gas industry which was not convinced of the scientific validity of the evacuation levels. As a result of this concern, and two meetings held between ERCB, Government, and Canadian Petroleum Association (CPA) representatives in 1986, a new Ad Hoc Committee on $H_2S$ was struck to review the specific evacuation levels and the scientific rationale for each.

# Terms of Reference

The specific terms of reference for the committee were:

1. To assess the scientific evidence for low level acute, subchronic and chronic effects of $H_2S$ on humans in the range 0 to 100 ppm, and especially the 0 to 20 ppm range.
2. To clarify the issue of the effects of low levels of $H_2S$ on sensitive individuals. The committee was asked to submit its final report to Alberta Community and Occupational Health, who would use it to develop evacuation guidelines for Albertans during uncontrolled sour gas releases.

The members of the committee were:

Dr. David Chisholm, Past Chairman, Health Committee, Canadian Petroleum Association

Mr. Geoff Granville, Manager of Toxicology and Material Safety, Shell Canada Ltd.

Dr. Don Johnston, Medical Consultant,University of Calgary

Dr. Bob Rogers, President, Toxcon Consulting Ltd.

Mr. Ed Collom, Assistant Director, Environmental Health Services, Alberta Health (ex officio)

The committee undertook an extensive literature review and, where possible, obtained original articles, abstracts and review papers. Definitive data from well-designed studies were weighed against more anecdotal observations in the search for good end points from which conclusions could be drawn. The review included a comparison of animal research data, human experimental data and human epidemiological studies.

In conducting its critical assessment, the committee relied heavily on its collective technical knowledge of the health effects of $H_2S$, as well as its professional judgment in areas where the scientific literature was not as strong as would be preferred.

# I. Introduction

Hydrogen sulphide ($H_2S$) at high concentrations (>700 ppm) is extremely toxic to animals and humans, causing death in minutes to hours (Haggard, 1925; Yant and Fowler, 1926; Evans, 1967). By contrast, at concentrations that have been encountered by the public (<50 ppm), $H_2S$ may cause adverse effects in humans but these have generally been reversible and not lethal (Mitchell and Davenport, 1924).

Concern has been raised about the potential for adverse health effects on the public as a result of exposure to $H_2S$, the predominant sulphur compound in sour gas. There have been many instances of uncontrolled sour gas releases, as well as controlled flarings, in Alberta since the development of the oil and gas industry, but concerns peaked during the Lodgepole blowout in 1982. As a result of this, several provincial government agencies and the petroleum industry have been developing emergency procedures to reduce future risks to the health of Albertans exposed to sour gas.

Sour gas includes a mixture of organic and inorganic compounds other than $H_2S$, and this mixture may make certain members of the public more susceptible to the effects of $H_2S$, even though the compounds may be present in smaller concentrations than $H_2S$. The committee recognizes that any assessment of health risks to the public must take the effects of such mixtures into consideration.

Numerous factors have been reported to influence the severity of the effects of $H_2S$ on humans, including health status, gender, age, individual susceptibility, interactions with other chemicals (e.g. drugs, alcohol, smoking), exercise level, nutrition, et cetera (NRCC, 1981; NIOSH, 1977; NRC, 1979), and frequency of exposure, exposure duration, and ambient $H_2S$ levels (Stolpe et al, 1976; Melnichenko, 1968; Ahlborg, 1951).

# II. Scientific Issues

Because certain scientific terms have different meanings for various disciplines, and in order to allow for consistency in interpreting the literature, drawing conclusions and making recommendations, such terms have been defined for the purposes of this report.

In addition, there are several principles or scientific issues with which the reader should be familiar so that the committee's approach to this task and our conclusions are clearly understood.

## A. Sour Gas

Sour gas refers to the raw natural gas mixture that is drawn directly from a geologic formation and is contaminated with various sulphur compounds including $H_2S$, mercaptans, carbon disulphide, dimethyl sulphide, et cetera (NRCC, 1981; NRC, 1979). In Alberta, $H_2S$ is the predominant sulphur contaminant of sour gas. Depending upon the particular geologic formation, the proportion of $H_2S$ may range from as little as <1 percent to over 90 percent[1]. Generally speaking, the other sulphur contaminants are present at concentrations at least one hundred times lower than $H_2S$, although it should be noted that only limited analyses of sour gas from various wells have been published.

The composition of a released plume of sour gas will change with time, due to the effects of atmospheric processes such as photo-oxidation, chemical decomposition, or reaction with other atmospheric gases (e.g. ozone, oxygen, nitrogen dioxide). The gas remains resident in the atmosphere from about 1 day to 40 days, depending on the season (i.e. temperature), latitude and atmospheric conditions. The primary chemical transformation of $H_2S$ in the atmosphere is oxidation by oxygen-containing radicals to sulphur dioxide ($SO_2$) and sulphates. These reactions have been reviewed by Andersson et al (1974). Carbon disulphide, on the other hand, is most likely converted to its oxidized form, carbonyl sulphide (COS), in a similar fashion.

Although $H_2S$ is the predominant sulphur contaminant in sour gas, the minor sulphur contaminants may act with $H_2S$ to increase the severity of biological response to $H_2S$. The severity of a response to sour gas would ultimately be determined by the toxicity of each contaminant and not just the quantity. For example, certain compounds (e.g. cyanide) are extremely toxic in minute quantities. Thus, quantity must not be the overriding factor when considering the potential toxicity of a mixture.

## B. Health

As indicated previously, one of the main concerns of not only the public but also the ERCB in its inquiry was the question of the effects of sour gas on human health. But the term "health" can be defined many ways, from purely physiological effects to psychological ones, so it is important to define the term "health" before starting to discuss health effects.

The committee felt that the World Health Organization's (1946) definition of health is the most appropriate for the purposes of this report:

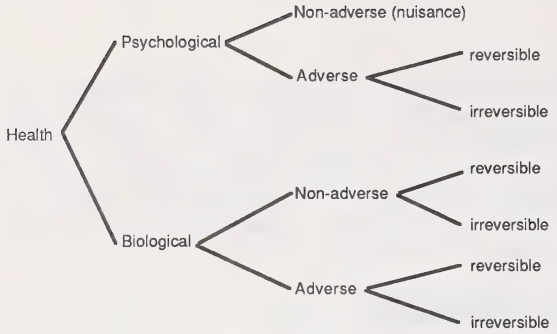
> "Health is a state of complete physical, mental and social well-being, not merely the absence of disease or infirmity."

Obviously, if evacuation limits were developed using this definition in its strictest sense, then any odor that disturbed individuals or communities could result in some "action" being taken, the most extreme being evacuation.

The committee realized that any bad-smelling sulphur release alters, temporarily at least, the quality of life. The issue of concern here was whether any irreversible adverse health effects are likely to occur as a result of such an exposure. A review of temporary, reversible effects was not included in this report since it was felt that society would perceive such effects as much more "acceptable" than irreversible ones.

Since the odor threshold for $H_2S$ is 3 or 4 orders of magnitude lower than that which may cause irreversible adverse health effects, the committee divided the term "health" into a psychological component consisting of both non-adverse (nuisance) and adverse (e.g. irritability, depression, lethargy) effects, and a biological component, also consisting of adverse and non-adverse effects. This can be summarized as follows:

[1] 1 percent $H_2S$ = 10,000ppm




# C. Effect

According to the Concise Oxford Dictionary, an "*effect*" is a "result or consequence" (Fowler and Fowler, 1964). A "*health effect*," therefore, refers to a certain health consequence. Bernard and Lauwerys (1986) take this one step further by defining a *biological effect* as a "biochemical, functional or structural change resulting from the reaction of an organism to the exposure." Such a change is considered *non-adverse* if it does *not* involve an impairment of functional capacity, a decreased ability to compensate for an additional stress, a decreased ability to maintain homeostasis, or an enhanced susceptibility to other environmental influences. It follows then that an *adverse biological effect* is the result of a negative impact on the foregoing criteria. However, adverse biological effects can be *reversible*, as in the case of the return to normal vision following blurred vision or eye irritation, or decreased coughing following removal of a throat irritant. These effects may also be *irreversible*, as in the case of irreparable tissue damage (e.g. emphysema induced by excessive cigarette smoking). From the previous diagram, it can be seen that these terms may also apply to adverse psychological health effects, so it is very important to distinguish between adverse biological and adverse psychological effects of $H_2S$ on people.

# D. Susceptibility/ Hypersusceptibility, Sensitivity/ Hypersensitivity

One of the committee's terms of reference was to clarify the issue of $H_2S$ effects on individuals who might be considered to have a higher degree of "sensitivity" to $H_2S$ at low levels than other members of the population. In order to do this, it was first important to define what was meant by "sensitivity." Bernard and Lauwerys (1986) proposed a definition which mentioned "enhanced susceptibility" as a key criterion of an adverse biological effect. This terminology creates some difficulty since the term "sensitivity" is used synonymously and interchangeably with the term "susceptibility" and pervades both the scientific literature and existing documentation in Alberta. In 1982 a symposium was held in the United States to attempt a definition of the so-called "sensitive" individual (Baier, 1982). The basis for holding the symposium was the recognition of the inherent biological variability in the response of a human population to the same dose of a chemical. Some of the reasons for this lie in variations in lifestyle, current and past exposures, current health status, and genetic susceptibility. Although the terms "susceptibility" and "sensitivity" are used interchangeably, there are subtle and important distinctions between them. According to Buffler (1982), a "sensitive individual" is one who responds readily and intensely to an exposure, whereas a "susceptible individual" refers to "one who has the capacity or disposition to develop disease or be physically affected." The increase in sensitivity and susceptibility is often indicated by the prefix "hyper," which implies that responses of these individuals is quantitatively or qualitatively greater than a "normal" individual.

According to the Merriam-Webster dictionary, the definition of "susceptible" is "having such a constitution or temperament as to be open, subject or unresistant to some stimulus, influence or agency; having little resistance to a specific infectious disease; predisposed to develop a noninfectious disease; abnormally reactive to various drugs." Since, in theory, any compound given in a high enough dose will produce a toxic effect in any given person, everyone is really "susceptible" to an adverse biological reaction to any environmental agent. Given the comprehensive definition above, use of the term "hypersusceptible" then seems superfluous. For this discussion, therefore, the term "*hypersusceptible*" will be reserved for persons whose constitution causes them to be abnormally reactive to the greatest extreme (Murray, 1986). In other words, their susceptibility to a given exposure is several orders of magnitude greater than that of the usual class of susceptible persons.

Returning now to the term "sensitivity," toxicologists often use it to define an immunologic, sensitization reaction which is dose-related, involves only a fraction of the exposed population,

and requires pre-exposure of an individual to elicit the acute immune response (Klassen et al, 1986). The term "*hypersensitivity*" will, therefore, be used to refer to an immunologic reaction that is several orders of magnitude greater than that of the non-sensitized individual.

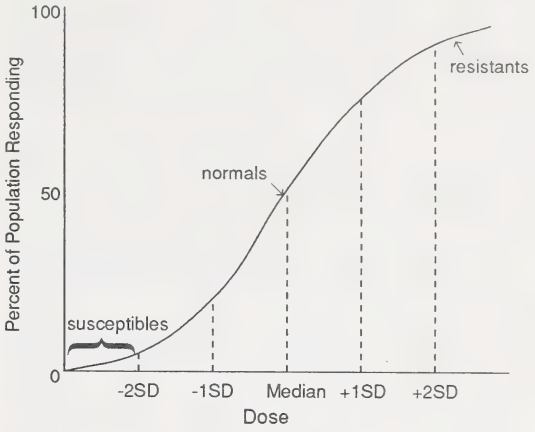
Given these definitions, we might conclude by stating that "All sensitives are susceptible but not all susceptibles are sensitive."

# E. Dose-Response Relationship

The rationale behind the setting of specific emergency action levels is based on a fundamental toxicological concept, the dose-response relationship. According to this principle, individuals in a population may differ in their response to an increasing dose of toxic substance. These individual responses contribute to a population dose-response curve, on which the percentage of the population responding with a given effect is plotted against dose. Those who react at low doses are thus the first to respond and contribute to the building of the curve. The percent of individuals in a normal Gaussian population falling into this category is usually less than 5 percent (i.e. >2 standard deviations), with the hypersusceptibles and hypersensitives making up a smaller proportion of this percentage (Murray, 1986; Ashford, 1986; Loomis, 1974). The so-called "normals," on the other hand, would comprise 95 percent of the population (±2 standard deviations), while at the upper extreme a small percentage (approximately 2-3 percent) of individuals would be very resistant to the exposure or not respond at all. This is summarized in Figure 1 in the cumulative frequency curve.

Note that the curve does not illustrate the existence of a "threshold" for an adverse response. For most chemicals, except for carcinogens, it is generally accepted that a threshold exists defining the minimum dose necessary to exceed the body's capacity to compensate for the additional stress and maintain homeostasis. For $H_2S$, specifically, the threshold for adverse effects (i.e. the Adverse Effect Level or AEL) has yet to be determined for humans, although PACE (1985) reported that a Federal Committee has placed this level at 1.0 ppm. It is important to note, however, that an individual's threshold can vary considerably from that of the population. The best example here, of course, would be the hypersusceptible individual who could be expected to begin responding in the parts per billion range of $H_2S$, which is much less than the population threshold.

**Figure 1. Typical cumulative frequency response curve for a normal population**




Another point worth noting is that those persons considered to be hypersusceptibles may or may not be in a high-risk group. A high-risk group by definition would be a group of individuals who are inherently more likely to respond to a given level of $H_2S$. Reasons for this might include that they may have been exposed previously, or have an existing or prior disease (e.g. cystic fibrosis), or may have an immature or compromised physiological status (e.g. very young or old), or have a variety of other characteristics, including hypersensitivity. The underlying causes of variability in susceptibility and variability of high-risk status are complex. Compounding this complexity is the fact that susceptibility is not static. Numerous factors (e.g. age, nutritional, hormonal and immunologic status) can shift a previously normal individual into the hypersusceptible or high-risk categories or vice versa (Ashford, 1986). This is important in the present exercise since it means that one must determine clearly from the outset what segment of the population specific action levels are meant to protect, that is, high-risk groups only, hypersusceptibles only, a combination of the two, or the entire population. The greatest difficulty from a practical standpoint will be in the identification of individuals in each of these groups, particularly the hypersusceptibles because we do not know all the factors that might make individuals hypersusceptible to $H_2S$.

One final aspect that deserves attention when discussing dose-response relationships is the assumptions upon which the relationship rests. They are as follows:

1. The response is related to the concentration of the toxic agent at the receptor site.

2. The concentration of the toxic agent at the receptor site is related to dose.
3. Response and dose are causally related.

With respect to the last point, a series of criteria should be fulfilled to establish a causal relationship in a population. According to Murray (1986), these include:

1. A strong association between the environmental agent and specific health effect should be clearly established.
2. When the environmental agent is removed, the effect should diminish or completely disappear.
3. The association should be demonstrable by more than one investigator (i.e. reproducible).
4. The effect observed should be biologically plausible.
5. The temporal (time-related) sequence of the exposure and abnormal effect should be clear and unambiguous.
6. Animal experiments, if there are any, should be consistent with the cause and effect in humans.
7. The result of exposure of susceptible individuals to the environmental agent should be specific (i.e. unique in quality or quantity).
8. A biological gradient should exist between exposure and effect.

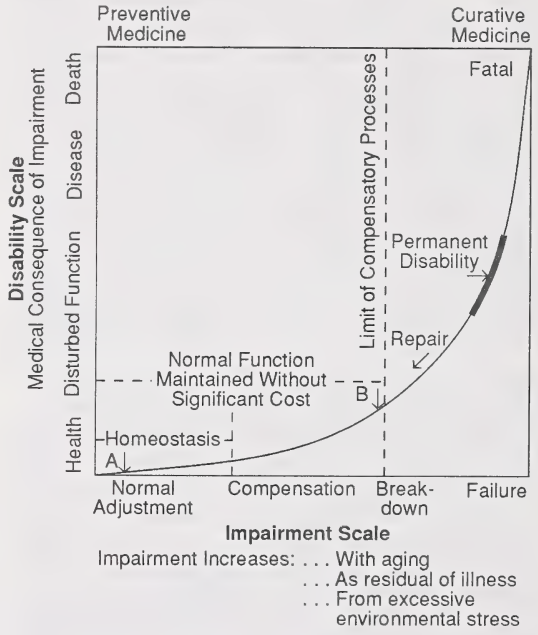
# F. Homeostasis

Bernard and Lauwerys' (1986) definition mentions decreased ability to maintain homeostasis as another key criterion of an adverse biological effect. What is meant by the term "homeostasis"? Wood (1978) defines homeostasis as the "tendency for an animal to maintain itself in a given condition, or steady state." Most animals possess a number of homeostatic mechanisms designed to keep their internal environments constant, among them energy release and utilization, osmotic and ionic regulation, temperature regulation, excretion, et cetera. Briefly, most physiological mechanisms have a certain range (i.e. the "normal range") in which they can operate without adversely affecting the animal. Homeostatic mechanisms merely regulate internal events (e.g. metabolism) to maintain the internal environment in the normal range. If this range is exceeded this does not automatically mean that the animal cannot continue to function normally since each animal or organ has a "reserve functional capacity" to maintain normal function without significant cost. An example of this is the fact that humans can still function normally with only one kidney, or part of a lung or liver. This is best illustrated as the zone of "compensation" in Figure 2.

# G. Multifactor Relationships in the Etiology of Disease

Hatch (1963) summarized the multifactor relationships in the etiology of disease in the following diagram.

**Figure 2. Multifactor relationships in the etiology of disease.**




Note that the zones of normal adjustment and compensation will permit normal function to be maintained without significant cost. Also note that the body is equipped with repair systems so that even as point B (the threshold for breakdown and disturbed function) is exceeded, these systems will operate to bring function back into the normal range. However, if an excessive environmental stress continues, then permanent disability (e.g. irreversible tissue damage) may result. If this progresses, disease may be the result, and finally, if left unchecked, death can occur.

The foregoing figure is important in the

setting of any numerical action level because it demonstrates the multifactoral basis for the development of disease. The principles underlying the curve are, in fact, perhaps the most misunderstood by the general population who are suddenly faced with an uncontrolled release of $H_2S$. During the ensuing increase in anxiety over such an event, communicators with the public have failed to transmit clearly that exposure to a low concentration of $H_2S$ does not automatically put individuals in the permanent disability or disease region of the curve. This is particularly true for $H_2S$ because it is rapidly oxidized in the blood (Haggard, 1921), so the dose encountered by the target organ will probably be several orders of magnitude less than the ambient concentration of $H_2S$. Thus, a period of normal adjustment or compensation will typically occur. This, of course, is not an atypical response of the body following exposure to environmental agents. It occurs routinely every day as our bodies respond to the chemicals comprising our food, the air we breathe, or the water we drink. Even if the level of "disturbed function" is reached, physiologic processes will tend to return to normal when exposure is ended. Thus, the biological significance of the alteration in the serum activity of a given enzyme, for example, should not be seen as a significant health risk to the individual. However, there would be cause for concern if this abnormal activity level did not return to normal when exposure ended, since this would indicate organ malfunction.

The form of the curve in Figure 2 may be altered if more than one chemical is present. In this case, effects may be synergistic, additive, potentiative or antagonistic.

# H. Acute and Chronic Toxicity

As previously stated, exposure duration can influence the severity of response to $H_2S$. Thus, prolonged exposure to a low concentration of $H_2S$ may produce the same adverse biological effect as a larger dose over a shorter period of time. For example, death in humans can result from exposure to 100 ppm for 8-48 hours or 1000 ppm for a few minutes (NRCC, 1981). These exposure and effect relationships need to be defined before setting emergency action levels.

According to WHMIS (1985), a "*chronic adverse health effect*" is one that "develops over time from a single exposure, or develops from prolonged or repeated exposure under conditions that do not produce the effect from a single exposure." Berylliosis is an example of the former, while silicosis is an example of the latter (Robbins and Angell, 1976). Since $H_2S$ is rapidly detoxified in the blood (Haggard, 1921; Evans, 1967), instances of the first type of chronic adverse health effect are rare. However, when repeated exposure to low levels of $H_2S$ has occurred, certain "chronic" effects have been reported. Included in this category are neurasthenic effects (Ahlborg, 1951; IIEQ, 1974), altered brain metabolism (Savolainen et al, 1980; Haider et al, 1980), reproductive effects (Barilyak et al, 1975), skin disorders (Benini and Colamussi, 1969), et cetera.

At the other end of the spectrum is the "*acute adverse health effect*" which may be defined as the effect(s) produced as a result of a single exposure (i.e. less than 24 hours) to a high concentration of a toxic agent. Usually the effects are produced immediately and the severity of the effect is intense. For $H_2S$, acute toxicity results from a single exposure to a massive concentration (e.g. >700 ppm) of $H_2S$. This produces systemic poisoning, characterized by rapid onset and predominance of signs and symptoms of nervous system involvement, e.g. convulsions, respiratory paralysis, unconsciousness (NRC, 1979).

In "subacute $H_2S$ intoxication," on the other hand, "signs and symptoms of eye and respiratory tract irritation prevail" (NRC, 1979). Although subacute symptoms can follow a single brief but intense exposure, subacute effects are more often related to exposures of several minutes to hours. For example, 50 to 100 ppm $H_2S$ produces eye irritation within several minutes and respiratory tract irritation in 30 minutes (Milby, 1962).

The primary concern here is with irreversible adverse biological effects produced by $H_2S$ exposures between 0 and 100 ppm, with particular emphasis on the 0 to 20 ppm range. Note that while response to the odor of $H_2S$ will also occur in this range, the committee considers this to be largely a nuisance reaction (i.e. a non-adverse psychological response), especially at concentrations below 1.0 ppm. As such, the health risk to humans should be correspondingly low. However, hypersusceptible individuals may respond acutely to a concentration of $H_2S$ which in "normal" individuals would not produce clinical signs or symptoms.

# I. Epidemiology

Most scientific literature concerning the health effects of $H_2S$ covers toxicologic studies of $H_2S$ on animals. Documented human exposure experiences are, with few exceptions, about acute

exposure to high concentrations and usually involve fewer than five people. Reports of larger numbers of humans exposed to low levels of $H_2S$ are mainly anecdotal even though they have the tone of an epidemiologic study. As well, those anecdotal reports are about short term effects like dry eyes, nausea, and sore throats. Long term effects from low level exposure could be studied in detail at natural geothermal sites which have high concentrations of $H_2S$, like the city of Rotorua, New Zealand. Unfortunately, epidemiologic studies have not been conducted to investigate possible beneficial or harmful effects of living in such an environment, even though the residents perceive the geographic setting as healthful, as is evident by the presence of the State Arthritis Hospital and several holistic health offices in Rotorura.

In the absence of low level epidemiologic studies, human health effects must be estimated from animal toxicology and the health records of survivors of high concentration exposure. Extrapolation of animal data to estimate human health effects is one of the most controversial aspects of risk assessment, particularly when the requirement is to protect human health at low concentrations. Although animal toxicology data is precise in comparison to what might be available from human epidemiologic studies, the data can seldom provide the same amount of valid information as epidemiology.

The cornerstone of epidemiology is the identification of unusual occurrences of disease. Yet the population studied is composed of individuals who may be genetically different, eat different foods, perform different jobs, and live in different conditions, all of which produce a variety of environmental exposures. There are additional confounding factors, like smoking, which may affect the incidence of a disease in a population in different ways. For example, Japanese men smoke as much as North American men, yet they have a much lower incidence of heart disease. Is this due to a genetic difference or to dietary differences between the two groups?

Epidemiologic studies of environmental factors and health are limited by the lack of good early markers for disease. Developments in the biosciences will improve this situation and contribute to more valid data with which to study the health of a population.

Cause and effect are rarely identified by epidemiologic studies. More common is an association between an exposure to an agent and a disease. Heart disease, for example, is associated with a high animal fat diet, yet animal fat is only one of several factors contributing to the development of heart disease.

One of the main contributions from epidemiologic studies of environmental factors is the reassurance for the public that there is no excess of disease. Large studies of VDT operators and pregnancy have been reassuring about the safety of this type of work for pregnant women. At times the public is not convinced, regardless of the scientific findings. The Love Canal studies, for example, were conducted with a large amount of data about very toxic chemicals to which the population could have been exposed. The lack of evidence of adverse human health effects has not reassured many residents of the area. Some scientists use this example to illustrate the limitations of epidemiology. Based upon their knowledge of the effects of the chemicals on animals, they feel that there must have been human health effects but that the studies failed to detect them. Other scientists interpret the same information as evidence that our perceptions about the human health effects of environmental agents are the result of an histrionic press and not reality.

The implications for this report are that effects on human health of low concentrations of $H_2S$ can only be estimated at present. Until large epidemiologic studies are conducted with a valid estimate of $H_2S$ exposure, we must extrapolate from:

1. Animal toxicology.
2. Acute high concentration human exposures.
3. Anecdotal reports like those from Rotorura and the Lodgepole blowout.

# III. Review of Critical Studies on $H_2S$

The terms of reference for the committee were to assess the scientific evidence for adverse effects of $H_2S$ on humans in the 0 to 100 ppm range, with special emphasis on the 0 to 20 ppm range. Given the time and resource constraints for the project and the extensive body of literature on $H_2S$, an attempt was made to select only critical studies for review. Studies were selected on the basis of the following criteria:

1. Human data was preferable to animal data.
2. Severity of adverse biological effects (e.g. untreatable lung cancer is more severe than irritant dermatitis).
3. Quality of ambient monitoring data.
4. Existence of a dose-response relationship.
5. Reproducibility of the effect.
6. Design of the study (e.g. controlled study better than ad hoc survey or anecdotal information).
7. Biological plausibility of the effect following exposure to $H_2S$.
8. Temporal sequence of exposure and effect should be clear and unambiguous.
9. Similarity of exposure conditions to potential conditions arising from uncontrolled sour gas release.

One point is worth noting in relation to the use of animal data and its extrapolation to humans. Early workers studying the effects of $H_2S$ on animals (Mitchell and Yant, 1925; Haggard, 1925; Sayers et al, 1923) noticed that the effects were the same as those observed in humans (Lehman, 1892). The NRC (1979) summarized data derived from Sayers et al (1923) to illustrate this point in Table 1.

On the basis of this data, NRC (1979) concluded that animals in general respond similarly to humans to equivalent concentrations of $H_2S$, perhaps even down to the level of insects. For the purposes of this exercise, therefore, when animal data has been used, a 1:1 correlation between animals and humans has been assumed at high concentrations unless data exists to the contrary.

In order to identify hypersusceptible individuals or potential high-risk groups, the committee has reviewed the effects of $H_2S$ on a system by system basis.

**TABLE 1. CONCENTRATIONS OF $H_2S$ RESULTING IN SUBACUTE OR ACUTE INTOXICATION SYNDROMES IN VARIOUS SPECIES**

| Species | Subacute Syndrome (Concentration of $H_2S$ in ppm) | Acute Syndrome (Concentration of $H_2S$ in ppm) |
|---|---|---|
| Canaries | 50-200 | ≥ 200 |
| White rats | 50-550 | ≥ 500 |
| Dogs | 50-650 | ≥ 600 |
| Guinea pigs | 100-750 | ≥ 750 |
| Goats | 100-900 | ≥ 900 |
| Humans | 100-600 | ≥ 600-1000[2] |

## A. Eye

Because the moist mucous membrane of the eye is exposed directly to the atmosphere, it is very susceptible to the irritant action of $H_2S$. For humans, concentrations at which eye effects occur have been variously reported as 100 ppm (Deveze, 1956), 30 ppm (Yant, 1925; Barthelemy, 1939), 20 ppm (ACGIH, 1984), 15 ppm (ACGIH, 1984), above 10 ppm (ACGIH, 1984), 10 ppm or even 5 ppm (Elkins, 1950), 4 to 15 ppm (Masure, 1963), 0.7 ppm (Rubin and Arieff, 1945; Lewey, 1938), 0.088 ppm (Kleinfeld et al, 1964), 0.02 ppm (USPHS, 1964), 0.0009 ppm (Duan, 1959; Baikov, 1963), and 0.004 ppm (Loginova, 1957).

The current Alberta occupational exposure limit (OEL) for $H_2S$ is 10 ppm. Like ACGIH, the basis for this OEL is primarily the greater incidence in irreversible eye tissue damage at concentrations ≥20 ppm for several hours' exposure. For example, at concentrations greater than 50 ppm for 1 hour, irritation and inflammation of the conjunctival and corneal tissues may occur, a condition called "gas eye" (Milby, 1962; Gosselin et al, 1976).

As acute conjunctivitis develops, characteristic signs and symptoms include pain, mucopurulent discharge, tearing, hyperemia, retroorbital aching, blepharospasm, blurred vision, photophobia, and the illusion of rainbow-like colors around incandescent lights (Beasley, 1963). As this condition progresses, vesiculation and ulceration of the corneal epithelium may result in scar formation and permanent impairment of

[2] immediately lethal

vision (Mitchell and Yant, 1925; Yant, 1930; Gosselin et al, 1976).

At $H_2S$ concentrations below 50 ppm, longer exposure is required to elicit the same effects. For example, Nordstrom and McQuitty (1975) concluded that permanent corneal tissue damage could be elicited in calves exposed to 20 ppm for 7 days. Others have reported inflammation of eye tissues (spinner's eye) after 6-7 hours of exposure to 11 to 21 ppm $H_2S$ (Elkins, 1939; Nesswetha, 1969). However, as pointed out in the NIOSH (1977) document, other stressors such as noise, thioformaldehyde, and other irritating chemicals were present and likely contributed to increased susceptibility to eye irritation by $H_2S$.

It is important to note that irreversible eye tissue damage has not been reported in subchronic studies of mice and rats exposed to 10 ppm $H_2S$ (6 hours/day, 5 day/week for 90 days — CIIT, 1983). However, other investigators have reported variable eye effects in humans at $H_2S$ concentrations $\leq$ 10 ppm. For example, decreased corneal reflex has been reported to occur at 0.7 ppm (Rubin and Arieff, 1945; Lewey, 1938), blurred vision at 0.08 ppm (Kleinfeld et al, 1964), increased sensitivity to light at 0.008-0.009 ppm (Duan, 1959; Baikov, 1963), burning eyes at 0.02 to 0.03 ppm (USPHS, 1964), and "vision problems" at 0.004 to 0.21 ppm (Loginova, 1957).

The biological significance and reversibility of these effects has yet to be determined experimentally, but it appears that no irreversible effects have occurred at $H_2S$ concentrations of less than 1.0 ppm (NRC, 1979; NRCC, 1981; WHO, 1981).

The presence of other gaseous pollutants, especially carbon disulphide ($CS_2$), and humidity are believed to increase the effect of $H_2S$ on the eye (Barthelemy, 1939; Masure, 1950). For example, Barthelemy noted that eye injury was avoided if $CS_2$ and $H_2S$ concentrations were kept below 30 ppm and 20 ppm respectively. The mechanisms by which $CS_2$ increases the susceptibility of the eye to $H_2S$ is still unknown. It is also noteworthy that finely atomized particles of $H_2SO_4$ were present in the workers' atmosphere and hence probably also contributed to the lowering of the threshold at which $H_2S$ causes irritation of the eyes. Again, these results need to be explored further experimentally.

To conclude, then, irreversible eye tissue damage can occur at 20 ppm $H_2S$, but on the basis of animal data, not at concentrations <10 ppm. Although several different effects have been reported in humans at concentrations <1.0 ppm, it appears, in the absence of evidence to the contrary, that these are reversible. Increased susceptibility to $H_2S$ in the presence of other vapors, however, should not be ruled out, as might occur in uncontrolled sour gas releases.

# B. Respiratory System

Since the mucous membranes of the respiratory system are also exposed directly to the atmosphere, they, too, are highly susceptible to the irritant effects of $H_2S$ which, because of its moderate solubility (Haggard, 1925), can penetrate to the alveolar level. Pulmonary tract irritation can be a more serious reaction than eye irritation, since in severe cases it can lead to pulmonary edema. If left unchecked, this could result in secondary pulmonary infections and, ultimately, death. At concentrations of >100 ppm, respiratory tract irritation occurs in humans in a few minutes (Milby, 1962). However, at a concentration of 50 ppm, irritation effects (e.g. inflammation, dryness of nose, throat, larynx, and bronchi) take longer (i.e. 30 to 60 minutes) to become manifested (Mitchell and Yant, 1925; Ahlborg, 1951; Milby, 1962). Prolonged exposure at this level may result in bronchitis, rhinitis, pharyngitis, laryngitis, and pneumonia (Haggard, 1925). Symptoms associated with these conditions include hoarse throat, nasal secretions, cough, and shortness of breath.

Several reports exist documenting respiratory irritation in humans at concentrations in the 0.02 to 20 ppm range (USPHS, 1964; Benini and Colamussi, 1969; Ahlborg, 1951; Prouza, 1970; Lodgepole Proceedings, 1983; Bhambhani et al, 1985). In general, data in early studies is not useful for toxicological interpretation because of the inaccuracy of the monitoring methods (e.g. lead acetate paper) which probably under or overestimated the actual concentrations of $H_2S$ significantly. In some cases, pollutants other than $H_2S$ alone are present in the atmosphere (e.g. hydrocarbons, $SO_2$), and their influence on the reported effects is unknown.

Apart from the foregoing points, the signs and symptoms reported are still typical of respiratory effects observed at $H_2S$ levels above 20 ppm. The exception to the above is the work recently completed by Bhambhani et al (1985) at the University of Alberta. In these studies, normal, healthy male and female subjects were exposed to 0, 2.5, and 5.0 ppm $H_2S$ for 15 minutes followed by an intense exercise stress test. No significant cardiac or respiratory effects, reversible or irreversible, were reported for any subject. In fact, this also appears to be the case for all episodes where humans have been exposed, accidentally or

experimentally, in the 0 to 20 ppm range.

The general conclusion for humans, then, is that irreversible respiratory effects are unlikely to occur in this range for the average, healthy individual. This may not be so for high-risk individuals such as the very young or old or those with pre-existing health conditions such as emphysema, tuberculosis, viral pneumonia, bronchitis, and asthma (IIEQ, 1974). During the Lodgepole blowout, for example, a chart analysis revealed numerous adverse responses in respiratory patients when the ambient outdoor $H_2S$ concentration was between 0.1 to 0.5 ppm. Whether these were irreversible has not been determined. However, the validity of the design of this study was questioned at the Lodgepole Inquiry.

In animals, most of the evidence supports the human data. For example, in a well-designed study, CIIT (1983) reported no respiratory effects of $H_2S$ on mice and two strains of rat at 10 or 30 ppm. These findings are generally supported by other investigators (Stolpe et al, 1976; Hays, 1972; Curtis et al, 1975; Weedon et al, 1940).

In a few instances, however, abnormal effects have been reported. Sandage (1961) reported lung pathology in 33 percent of a test group of rats exposed to 20 ppm for 90 days (continuous exposure), as well as abscesses of the lung and bronchopneumonia. Changes in the activity of several lung cell enzymes has also been reported for lung homogenates exposed in vitro (Husain, 1976; Husain and Zaidi, 1977). Slight irritation of the mucous membranes of the trachea and bronchi have also been reported in rats exposed to 10 ppm $H_2S$ for 12 hours/day, 5 days/week for 90 days (Duan, 1959). The reversibility of these abnormal effects has not been established, largely because the experiments were not designed to test for recovery following $H_2S$ exposure.

# C. Skin

At high concentrations of $H_2S$ (e.g. 100 percent), exposure for 60 minutes reportedly produced darkening of the skin, spots, red mottles, and skin rash (Yant, 1930). In the 0 to 20 ppm range very few reports exist. In one report, oil refinery workers in a gas desulphurization plant were exposed continuously to $H_2S$ concentrations between 5 and 10 ppm. They displayed various chronic and relapsing skin manifestations (Benini and Colamussi, 1969). It is noteworthy, however, that $SO_2$ and lower aliphatic compounds were also present and the duration of exposure was not established. More anecdotal information is available from the Lodgepole blowout, where 13 out of 608 (2.1 percent) complaints received on a government telephone complaint line reported skin irritation or allergies believed to be caused by $H_2S$ in the range of 0.1 to 0.5 ppm.

In conclusion, the average, healthy individual is unlikely to experience irreversible skin effects following an acute or repeated exposure to $H_2S$ in the 0 to 20 ppm range.

# D. Olfactory System

It is known that high concentrations of $H_2S$ (>150 ppm) elicit paralysis of the olfactory nerve center and cause loss of the sense of smell (Yant, 1930). At concentrations between 50 and 100 ppm, prolonged exposure may also produce paralysis (NIOSH, 1977). A similar effect has been reported within minutes in normal adult males exposed to 1 to 5 ppm $H_2S$ (Schulz, 1984). There are anecdotal reports of decreased olfactory function from some workers who have experienced several high accidental exposures during their employment (Johnston, 1988). This effect is reversible and is not, therefore, considered to present a significant health risk to an exposed population.

# E. Cardiovascular System

At high concentrations (>700 ppm), $H_2S$ has been reported to cause transient changes in the electrocardiograms of acutely exposed individuals (Kaipainen, 1955; Hurwitz and Taylor, 1954; Kemper, 1966). In another report, Ahlborg (1951) observed a decrease in blood pressure in a 30-year old male accidentally exposed to $H_2S$. All individuals recovered with no recurrent problems. Other reported signs and symptoms resulting from exposure to high concentrations of $H_2S$ include increased arterial pressure, decreased heart rate, altered cardiac rhythm (Kaipainen, 1954), bradycardia, tachycardia, weakness or fatigue, and fainting (NIOSH, 1977).

Below 100 ppm Kosmider et al (1967) reported cardiac irregularities and decreased myocardial enzyme activities in rabbits exposed to 71 ppm $H_2S$ 0.5 hour/day for 5 days. These abnormalities were reversible with recovery occurring several days post-exposure. Hays (1972) observed no effect of $H_2S$ on heart rate or blood pressure in goats or cows exposed continuously for 4 days to 10 and 50 ppm (goats) or 20 ppm (cows) for 21 days. Similar results were reported in the CIIT (1983) study using mice and rats exposed to 10, 30 and

80 ppm $H_2S$ 6 hours/day, 5 days/week for 90 days.

In humans, this finding was also supported by Bhambhani et al (1985), who exposed healthy human subjects to 2.5 and 5.0 ppm $H_2S$ for 15 minutes and observed no effects on blood pressure or heart rate. Below this level, no cardiovascular effects have been reported either in humans or animals. Thus, it appears that $H_2S$ presents no significant cardiovascular risk to healthy adults at levels below 20 ppm. The USPHS (1964) investigation of the Terre Haute incident suggests, however, that individuals with heart disease may be in danger if exposed to low concentrations of $H_2S$. The scientific validity of this conclusion still needs to be established experimentally. Furthermore, the use of accurate measures of cardiac toxicity is required, since heart rate and blood pressure are imprecise.

# F. Liver

The hepatic effects of $H_2S$ have received little attention in animals and humans. Sava et al (1980) reported decreased bile flow in rats injected with 40 ug/kg (30 ppm) sodium sulphide. Weedon et al (1940) reported "pale, enlarged" livers in mice exposed to 63 ppm $H_2S$ for 16 hours. Bulatova et al (1968) studied 2,465 high-sulphur petroleum refinery workers in two different cities who were exposed to unspecified concentrations, with 601 machine-tool workers and 706 railroad workers as controls. The incidence of cholecystitis (gall bladder disease), cholangitis (bile duct disease), and cholelithiasis (gallstones) was greater in the oil refinery workers.

No effects were seen in mice and rats exposed for 90 days to 10, 30 and 80 ppm $H_2S$ (CIIT, 1983). Furthermore, no effects in humans have been reported as a result of short-term air pollution episodes. Thus, it would appear from the limited animal data that $H_2S$ presents no risk to humans in the 0 to 20 ppm range. In light of inadequate monitoring data, the Bulatova et al (1968) study is of limited usefulness other than to establish an area that needs further research.

# G. Kidney

The renal effects of $H_2S$ have also received little attention, especially in humans. In animals, Weedon et al (1940) reported "pale kidneys" in mice exposed to 63 ppm $H_2S$ for 16 hours. Sandage (1961) reported kidney pathology in 6 percent of his test animals exposed continuously to 20 ppm $H_2S$ for 90 days. CIIT (1983), on the other hand, reported no kidney lesions or abnormal clinical findings in mice and rats exposed for 90 days to 10, 30 and 80 ppm $H_2S$. Aitbaev et al (1976) found no changes in kidney succinate dehydrogenase activity in rats exposed to 7 ppm $H_2S$ for 6 hours/day, 5 days/week for 120 days.

Again, it would appear from this data that $H_2S$ in the 0 to 20 ppm range presents little health risk to healthy humans.

# H. Gastrointestinal System

Some of the most frequently reported gastrointestinal (GI) symptoms reported during exposure to $H_2S$ include nausea, "feeling sick," diarrhea, vomiting, and stomach cramps (pains). For example, during the Lodgepole blowout in 1982, these symptoms accounted for 55 percent of all telephone complaints received by the Alberta Government from residents of Edmonton. The ambient concentration of $H_2S$ for several consecutive days during this episode ranged between 0.01 to 0.50 ppm. A similar pattern of symptoms occurred during the Terre Haute, Indiana, air pollution episode. Here $H_2S$ levels ranged between 0.022 to 0.125 ppm for 7 consecutive hours (USPHS, 1964; NIOSH, 1977).

In all cases these symptoms ceased following cessation of exposure to $H_2S$. To date there appear to be no irreversible GI effects of $H_2S$ in humans, particularly in the 0 to 20 ppm range in which we are interested. The same holds true in animals where numerous repeated or chronic exposures have failed to turn up any irreversible effects (CIIT, 1983; Sandage, 1961).

# I. Immunological System

Very little research has been done to explore the effects of $H_2S$ on this system. Although there are a few reports in humans suggesting some form of immunologic reaction to $H_2S$, these lack the quantitative data necessary to test the causal nature of this relationship (Benini and Colamussi, 1969; Alberta Social Services and Community Health, 1983).

# J. Hematopoietic System

The effects of $H_2S$ on the hematopoietic system in humans has received little attention. Most of what is known about the effects on this system must be derived from animal studies.

Wakatsuki (1959) performed a study on rabbits in which the animals were exposed to 100 ppm $H_2S$ 30 minutes/day for 4 months. No change in the number of erythrocytes was noted; however, slight changes such as oligochromenia, reticulocytosis, leukopenia, and relative lymphocytosis were recorded. These quickly returned to normal after exposure stopped.

At lower concentrations (7 to 50 ppm), a number of changes have been reported. For example, Sandage (1961) reported increased leukocytes, hematocrit, hemoglobin, MCV, MCHb, and a decreased number of erythrocytes in mice exposed to 10 ppm $H_2S$ for 90 days. Stolpe et al (1976), on the other hand, noted no difference in blood cells in rats exposed to 10 ppm $H_2S$ for 41 days, while Melnichenko (1968) observed a 117 percent increase in the number of erythrocytes but no hemoglobin content change in rats exposed to 50 ppm $H_2S$ (and 300 ppm CO) for 4 hours/day for 6 months. Elebekova et al (1976) reported somewhat similar findings of increased erythrocytes, hemoglobin content, and leukocytes in rats exposed to 7 ppm $H_2S$ for 6 hours/day for 4 months. In addition, they noted increased eosinophils and neutrophils, slight reticulocytosis, decreased monocytes and erythrocytes. All of the above studies are in marked contrast to the subchronic study of CIIT (1983) on mice and rats where exposure to 10, 30 and 80 ppm $H_2S$ for 90 days revealed no effects of $H_2S$ on the hematopoietic system.

In light of these variable results, it seems that $H_2S$ in the concentration range 0 to 20 ppm may alter, temporarily at least, some of the blood constituents. Although the reversibility of this response still needs further research, it seems unlikely that it would be irreversible. Therefore, a significant health risk would not appear likely in the average, healthy adult. Individuals with severe anemia may constitute a high-risk group, since "the detoxification of $H_2S$ relies on the presence of oxygen in the blood and the amount of oxygen in the blood is dependent on both the amount of hemoglobin in the erythrocytes and on the number of erythrocytes" (IIEQ, 1974).

# K. Nervous System

$H_2S$ can produce either systemic or irritant effects depending on the concentration, duration and frequency of exposure. In the literature, numerous reports describe episodes of systemic poisoning. These have been reviewed a number of times (NIOSH, 1977; NRC, 1979; NRCC, 1981; Beauchamp et al, 1983; WHO, 1981). The threshold for systemic effects ranges between 500 to 700 ppm (Milby, 1962). In these episodes, general systemic effects predominate over local irritant effects. Symptoms of acute systemic intoxication include sudden fatigue, dizziness, intense anxiety, convulsions, loss of olfactory function, unconsciousness, collapse, and respiratory arrest followed by cardiac failure and death (Ahlborg, 1951; Mitchell and Yant, 1925). Recovery, if it occurs, is generally rapid and without sequelae (McCabe and Clayton, 1952; Ahlborg, 1951; Milby, 1962). If sequelae are reported, they are generally neurasthenic and may include fatigue, gastrointestinal disturbance, anxiety and depression, and peripheral acoustic neuritis. For example, Poda (1966) reviewed a number of acute cases and found a variety of symptoms (e.g. nervousness, dry, non-productive cough, nausea, headache, and insomnia) which lasted 1 to 3 days. Ahlborg (1951), on the other hand, in reviewing a number of cases in the oil shale industry, found that sequelae appeared immediately or shortly after the acute exposure and lasted approximately 1 to 1.5 months (although in one case some symptoms persisted for 3 years). The patients exhibited both neurasthenic symptoms (fatigue, drowsiness, headache, lack of initiative, irritability, anxiety, poor memory, decreased libido) and otoneurological symptoms (nystagmus, disturbances of equilibrium). It is noteworthy that a consistent finding in human and animal autopsies is significant brain tissue damage.

In contrast to acute $H_2S$ intoxication, poisonings in the 100 to 500 ppm range are characterized by signs and symptoms of irritation of mucous membranes of the eyes and respiratory tract. Nervous system involvement in subacute poisonings is indicated through the manifestation of symptoms such as headache, fatigue, irritability, insomnia, mild depression, and gastrointestinal disturbances (Milby, 1962). In the sole inhalation toxicology study to identify behavioral effects, Higuchi (1977) exposed rats to 100 to 500 ppm $H_2S$ and found that the discriminated avoidance response was significantly inhibited immediately after exposure to 200 ppm $H_2S$. After exposures to 300 to 500 ppm $H_2S$, both the discriminated and Sidman-type avoidance responses were inhibited at a rate and intensity paralleling the concentrations. Extinction of Sidman-type avoidance response was significantly accelerated only when the animals were exposed to concentrations over 500 ppm $H_2S$ (reviewed by Vigil, 1979).

Below 100 ppm, repeated exposures are usually necessary to produce symptoms indicative of nervous system involvement. The symptoms

associated with this so-called "chronic $H_2S$ poisoning" are generally neurasthenic (and hence subjective) in nature and include lethargy, dizziness, loss of appetite, fatigue, headache, mental depression, irritability, poor memory, abnormal peripheral reflexes, and gastrointestinal disturbances (Ahlborg, 1951; Rubin and Arieff, 1945). Ahlborg, in his study, cautions against the over-interpretation of his findings since most of the patients with these symptoms had probably been exposed previously to high concentrations of $H_2S$ or other substances. Hence, their neurasthenic symptoms may have merely been the sequelae of such poisonings rather than symptoms that could be considered true "chronic intoxication." Furthermore, although Ahlborg reported a higher frequency of neurasthenic symptoms in exposed versus unexposed worker groups at $H_2S$ concentrations around 20 ppm, he concluded that "it could not be determined whether this was caused by exposure to $H_2S$ (i.e. direct damage to the central nervous system) or whether such symptoms were manifestations of the psychic strain of working in an environment with a known risk of $H_2S$ exposure" (Vigil, 1979).

Several animal studies have attempted to explore the neurological effects of repeated exposure to low concentrations of $H_2S$. Sandage (1961) reported abscesses in the brains of mice exposed to 20 ppm $H_2S$ for 90 days. Haider et al (1980) reported a decrease in phospholipids and an increase in lipid peroxidation in the cerebral hemisphere and brain stem but no changes in the cerebellum of guinea pigs exposed to 20 ppm $H_2S$ for 1 hour/day for 11 days. Fatigue, somnolence, and dizziness were also reported.

Duan (1959) reported changes in the functions of the central nervous system (motor chronaxie abnormalities) and abnormal cerebral cortex dendrites in rats exposed to 7 ppm $H_2S$ 12 hours/day for 3 months. Exposures at 0.01 ppm for the same duration also produced slight motor chronaxie abnormalities. However, no pathological findings were reported in 2 rats when sacrificed and examined. No other nervous system effects were measured nor noted.

In another study conducted by CIIT (1983), exposure of mice and rats to 10, 30, and 80 ppm $H_2S$ 6 hours/day, 5 days/week for 90 days resulted in no abnormal behavior in the animals or pathological changes in nervous tissue.

At the biochemical level, however, a few studies have reported changes as a result of repeated exposure to $H_2S$. Savolainen et al (1980), for example, reported increasing inhibition of cerebral cytochrome oxidase activity following four successive exposures to 100 ppm $H_2S$ for 2 hours at 4 day intervals. This change was also accompanied by reduced orotic acid uptake, decreased cerebral RNA synthesis, reduced cerebral glutathione concentration, and decreased lyosomal acid proteinase activity. The authors of this study suggest that the cumulative nature of these effects might explain the increased headache frequency, increased fatigue, and slow deterioration of mental functions often reported in humans exposed repeatedly to $H_2S$ (NRC, 1979).

It would appear that repeated exposures to $H_2S$ can produce both pathological and biochemical changes in animal nervous tissue. The irreversibility of these changes is supported by three studies (Sandage, 1961; Haider et al, 1980; Duan, 1959) at $H_2S$ concentrations of 7 and 20 ppm; however, a fourth and more rigorous study (CIIT, 1983) reports no permanent changes in nervous tissue structure or function. In view of this conflicting evidence, the possibility exists that repeated exposure to $H_2S$ at levels between 5 and 20 ppm may cause irreversible nervous tissue damage in humans. This is something that needs further extensive research.

For concentrations of $H_2S$ below 5 ppm, little animal work has been done. In humans, however, Loginova (1957) reported that people residing near petroleum centers, where exposures to $H_2S$ were below 0.04 ppm, complained of odor, headache, nausea, tiredness, and other symptoms. It was noted however, that mercaptans, sulphides, disulphides, and other constituents of natural gas were present and, therefore, the signs and symptoms may not be solely attributable to $H_2S$. Nevertheless, the following dose-response relationships were developed by Loginova:

- 0.007 to 0.009 ppm $H_2S$: occupants of homes did not complain of headaches;
- 0.01 to 0.03 ppm $H_2S$: occupants complained of headaches only in response to investigator's questions;
- >0.04 ppm $H_2S$: occupants complained of headaches, general weakness, nausea, lack of endurance, and disturbance of vision.

Glebova (1950) reported that infants whose mothers worked in artificial silk factories — and who were exposed repeatedly to 0.02 to 0.04 ppm $H_2S$ via the mother's clothing during breast-feeding — showed retarded development, listlessness, anemia, and other symptoms. $CS_2$ did not appear to be present during breast-feeding. The fact that the signs and symptoms disappeared when the breast-feeding took place away from the plant and after a change of work clothes is strongly suggestive that $H_2S$ was the causal agent.

In 1964, the U.S. Public Health Service re-

ported that in the city of Terre Haute, Indiana, biodegradation of industrial wastes in a 14.5 hectares lagoon caused the atmospheric concentration of $H_2S$ to reach a 1 hour mean concentration of 0.3 ppm. Levels ranged between 0.022 and 0.125 ppm for 7 consecutive hours in some parts of the city. Again, these levels were measured using the lead acetate paper method and, therefore, the actual levels of $H_2S$ may have been considerably higher. During this incident, 81 complaints were registered, 41 of which were health-related. The most common health complaints included nausea, loss of sleep, headaches, and fainting. Investigators stressed that the odors emanating from the lagoon caused more than a mere nuisance (USPHS, 1964; NRC, 1979; WHO, 1981).

Schieler (1973) reported a correlation between mental depression in Washington State and chronic exposure to $H_2S$ in the 0.09 ppm range. The preliminary study used suicide, divorce rates, and psychiatric admissions to hospitals as indicators of depression and found that the highest rates correlated with the highest $H_2S$ distribution (IIEQ, 1974). This particular study has received little support, however, since numerous other socioeconomic factors or other air pollutants may have been involved.

In 1982, during the Lodgepole blowout in Alberta, a total of 608 health-related complaints were received in Edmonton. In descending order of frequency, the symptoms reported were headache (15 percent), nausea (14 percent), dizziness (1 percent), insomnia (1 percent), tiredness (0.8 percent), and other (0.8 percent — e.g. numbness, emotional disturbance, tingling limbs, double vision, loss of sense of smell). The range of $H_2S$ exposure during this episode was from 0.01 to 0.50 ppm.

It appears that in all of the aforementioned studies, the effects of $H_2S$ were reversible when exposure ended. Thus, repeated exposure to very low levels of $H_2S$ (<0.01 to 0.50 ppm) does not appear to produce any irreversible, adverse biological effects. However, caution must be exercised in the interpretation of this statement since in the absence of strong animal or human data in the <0.01 to 1.0 ppm range, it is not possible to rule out the existence of irreversible nervous tissue effects. This question is one that will require further experimental study.

# L. Psychological Effects of $H_2S$

An important extension of the question of CNS effects of $H_2S$ is its effect(s) on human behavior.

Approximate odor thresholds for $H_2S$ have ranged between 0.0005 to 0.36 ppm (Baikov, 1963; Leonardos et al, 1969).

Some possible psychological and physiological effects of $H_2S$ have been reviewed by Ryazomov (1962) and Kendall and Lindvall (1971). Kendall and Lindvall (1971) reviewed evidence relating to the ability of odorous substances to affect humans, either through disease states, annoyance reactions, social or economic reactions, and other physiological or psychological effects of unknown importance. They concluded that evidence to date has not demonstrated an effect of odor per se on either the cause or aggravation of disease. NRC (1979) also concluded, "There is, however, no evidence that the experience of malodor per se produces disease," but noted that poor health may increase the displeasure and thus frequency of complaints about an odor.

Odorous substances like $H_2S$ may, nevertheless, elicit a variety of physiologic effects at concentrations even below the odor threshold. Ryazonov (1962) identified several odor-caused reflexive responses besides the sensation of smell. These include changes in frequency and amplitude of breathing, contraction of the vocal cords and bronchial musculature, change in tonus of blood vessel walls, change in light sensitivity of the dark-adapted eye, change in the functional state of the cerebrum, and change in optical chronaxie. The last change involves the time threshold necessary for the appearance of a light sensation when a weak electrical current of necessary intensity to produce stimulation is applied to the eye. This latter effect indicates a decrease in visual responsiveness. The reversibility of these effects still remains to be established experimentally.

Thus, it would appear that repeated exposure to low levels of $H_2S$ may induce a variety of psychological and neurophysiological reactions. The psychological effects do not appear to enhance disease in an individual, while the significance of biological changes reported by Ryazonov (1962) remains ambiguous at present.

# M. Reproductive System

The reproductive effects of $H_2S$ in the 0 to 20 ppm range have received little attention. Some eastern European literature claims that long-term occupational exposure to $H_2S$ may have adverse effects on the menstrual and reproductive cycles in women and the subsequent development

of their children (Glebova, 1950; Vasil'eva, 1973; Barilyak and Vasil'eva, 1974; Barilyak et al, 1975). All of these studies suffer from poor reporting of results and more than one substance (e.g. $CS_2$, a known reproductive toxicant) was present and, therefore, the effects of $H_2S$ alone are still not known.

In their study on the effects of continuous exposure of rats to 7 ppm $H_2S$ (and 10 ppm CS2), Barilyak et al (1975) reported a pronounced embryolethal impact on females exposed before and during pregnancy, causing death of embryos in both the pre and post-implantation stages of development. Abnormalities of the genito-urinary systems, disturbance of embryonal blood formation and the ossification process, and severe changes in the parenchymatous cells of embryonic liver and kidneys were also reported. Again, the influence of CS2 in these responses is unknown since no $H_2S$ -only group was run.

In general, the effects of $H_2S$ on reproduction are still ambiguous and need to be corroborated by further studies. Since the blood rapidly detoxifies $H_2S$, it is unlikely that even the sensitive embryo would receive a sufficient dose in the 0 to 20 ppm range to cause adverse biological effects. As with other systems, however, the degree of susceptibility of the mother would be the key factor in assessing health risk to the developing embryo or fetus.

## N. Carcinogenicity, Mutagenicity, Teratogenicity

Very little evidence exists in the literature supporting any carcinogenic, mutagenic, or teratogenic effects of $H_2S$ in animals or humans.

# IV. Discussion

Based on the previous analysis of the scientific literature, it seems clear that some individuals may be more susceptible to the effect of $H_2S$ than others. Other factors besides dose and duration of exposure may in part account for hypersusceptibility of a small proportion of the population to $H_2S$ at low levels of exposure at any given time. These include:

a. mixed exposure with other chemicals at the same time (e.g. $CS_2$, CO, $CO_2$, $SO_2$, $O_3$, $NO_x$, $NH_3$, mercaptans or particulates) and/or recent exposure to chemicals in other settings (e.g. home, garden, work).

b. pre-exposure to medications, alcohol and/or other drugs.

c. pre-existing and/or current diseases, physiological conditions (e.g. nutritional/hormonal status), psychological status, and cardiovascular impairment.

While the committee recognizes that the following do not represent all possible situations where hypersusceptibility may exist, categories of individuals who may be expected to show increased susceptibility to $H_2S$ exposure include:

a. individuals with eye or respiratory tract problems — local irritant effects of $H_2S$ could aggravate pre-existing conditions (e.g. conjunctivitis, eye infection, tuberculosis, viral pneumonia, asthma, emphysema, bronchitis).

b. individuals with severe anemia — certain data indicate that detoxification of $H_2S$ requires the presence of adequate levels of oxygen in the blood.

c. individuals with lowered resistance to bacterial infections (e.g. immunosuppressed patients).

# V. Conclusions

1. $H_2S$ by itself is a broad spectrum toxicant that can elicit numerous psychological and biological responses in the 0 to 20 ppm range with which this review was concerned. As with any chemical, all organ systems respond variably to different levels of $H_2S$ with no given level affecting all systems equally at the same time or rate.
2. In general, single or repeated exposures of "normal, healthy adults" to $H_2S$ in the 0 to 5 ppm range have not resulted in clinically-detectable irreversible biological or psychological effects. Whether this is true for hypersusceptible individuals is not currently known. This areas needs further research.
3. Although reversible adverse effects may result in temporary discomfort or changes in organ function, they have not been found to have a lasting impact to date.
4. There are certain factors that may increase susceptibility of humans to $H_2S$ for which the scientific evidence is not strong. These include the use of alcohol (Poda, 1966; Beck and Donini, 1979); age, as in the case of the very young, the elderly or infirmed; and pre-existing cardiovascular disease (USPHS 1964).
5. There remains a lack of good scientific data about the long-term, low level chronic effects on community populations and on the work force in sour gas operations.

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# Appendix

The information in these tables has been extracted from the Final Task 4 Report prepared by the Midwest Research Institute for the U.S. Environmental Protection Agency, September, 1981. The tables have been updated where appropriate and modified to suit the needs of this exercise.

The intent of including these tables is to provide the reader with an easily accessible synopsis of existing scientific data. For more detailed questions arising out of this report, it is recommended that the reader refer to the original scientific papers.

TABLE 2. SUMMARY OF OCCUPATIONAL AND EPIDEMIOLOGICAL EXPOSURES TO $H_2S$

| $H_2S$ Level ($mg/m^3$) | (ppm) | Exposure Time | Effects | Reference |
|---|---|---|---|---|
| ≤28.4 >825 (and low concns. of HCN, $SO_2$, $CS_2$,hydro carbons) | (20–600) | Acute | Fatigue, dizziness, unconsciousness with or without respiratory failure. Rapid recovery (0.5 h) except for some nervous symptoms possibly lasting up to 1.5 mo. | Ahlborg (1951) |
| 326.6 | (230) | ~20 min. | Unconsciousness, cramping, slow and shallow breathing, and low blood pressure. Fully recovered in 6 mo. | Ahlborg (1951) |
| 40-185 | (29–132) | Acute, repeated | Within several hours, many signs of eye, nose, and throat irritation. Wide variation in individual responses. | Larsen (1944) |
| ~142 | (101) | — | Within several hours, many signs of eye irritation. A wide variation in individual response, light cases recovering in a few hours, and severe cases in a week. | Deveze (1956) |
| 13.7–36.6 | (10-26) | — | Eye irritation of varying severity, lasting from several hours to days. Some individuals had repeated episodes. | Kranenburg and Kessener (1925) |
| 15-35 | (11-25) | Acute | Nausea, weakness, and pain in the chest. Complete recovery within a week, no sequelae. | Prouza (1970) |
| 28.4 (often exceeded) | (20) | — | Fatigue, loss of appetite, irritability, headache, loss of memory, itching, and irritation of the eyes and respiratory tract. | Ahlborg (1951) |
| 7.1-14.2 (and $SO_2$ and lower aliphatic compounds) | (5-10) | — | Respiratory, gastroenteric, eye, and skin irritation. | Benini and Colamussi (1969) |
| 7.1-14.2 (and $SO_2$) | (5-10) | 5-15 y | Dermal symptoms suggestive of an allergic-type response. Some lung damage. | Benini and Colamussi (1969) |
| <14.2 | (<10) | — | Weakness, nausea, dizziness, headache, nervousness, and occasional unconsciousness | Podal (1966) |
| 0-9.94 | (0-7) | 3 d | Occasional slight and irregular changes in serum Fe and transferring levels and in fractions of urinary sulfates. | Benini and Colamussi (1969) |
| ~0.03–~0.43 (mixture) | (0.02–0.30) | 29 d Terre Haute, Ind. | Mild symptoms of nausea, vomiting, headache, shortness of breath, burning eyes, respiratory tract irritation, gastro-intestinal complaints, and disturbed sleep. | U.S.P.H.S. (1964) |
| 0.005–0.300 (mixture $CS_2$, $SO_2$) | (0.004–0.21) | Chronic | Headache, weakness, nausea, vision problems, and higher general morbidity rates in those households with ≥0.05 mg $H_2S/m^3$. | Loginova (1957) |
| 0.028–0.055 (mixture including $CS_2$, $SO_2$) | (0.02–0.04) | Chronic | Babies were poorly developed, underweight, listless, anemic, dyspeptic, and more susceptible to infectious diseases. | Glebova (1960) |

**TABLE 3. STUDIES OF OCCUPATIONAL EXPOSURE TO $H_2S$ (pg. 1 of 4)**

| Compound(s) Concentration(s) $mg/m^3$ (ppm) Duration | Population Group Description | Exposed | Controls | Effects | Remarks | Reference |
|---|---|---|---|---|---|---|
| $H_2S$ <28.4- > 825 (<20- > 600) Air levels varied with location. Also small amounts of $CS_2$, HCN, $SO_2$, and hydrocarbons | Shale oil plant workers | 54 "acute cases" | None | Symptoms included: a sudden feeling of fatigue, especially in the legs; dizziness; and intense anxiety followed by unconsciousness with or without respiratory failure. Pains in back of head, dizziness, and sometimes nausea followed regaining consciousness. Symptoms subsided in half an hour except in some case nystagmus (involuntary rapid eye movement) and Romberg's sign. Reflexes, coordination, eye movements, visual acuity, lungs, heart, blood, and blood pressure were normal. | Descriptive case study of clinical findings following relatively brief high concentrations of $H_2S$ mixed with a variety of gasline vapors. As a group exposures were poorly defined, but 7 case reports give exposure in great detail. Rates of symptoms and morbidity are not given for this group, although they would have been available. Therefore, the "risk" of unconsciousness, etc., is difficult to quantify from these data. There is some confusion between "acute," "subacute," and "chronic" exposures vs effects. Subacute exposure, p. 260, is defined as extremely intense, but brief. This is in fact a mild acute exposure with subacute effects or symptoms. Acute effects may follow chronic exposure and vice versa. | Ahlborg (1951) |
| $H_2S$ 326.6 (230) Exposure lasted ~20 min. | Worker in shale oil plant | 1M 30 y | None | Found unconscious, froth about mouth, cramps in right arm, slow shallow breathing, low blood pressure. He fully recovered in 6 d with no recurrence of symptoms over 2 y. | | Ahlborg (1951) |
| $H_2S$ ~40-185 (29-132) (from 5 single grab samples) | Workers building a tunnel | 50 | — | In 9 mo. 163 instances of eye irritation were seen half an hour to several hours after descending into the tunnel; burning, grainy sensation, and haloes seen around lights. The symptoms were not pronounced while in the tunnel, but increased when workers came out; photophobia, lacrimation, broken blood vessels and tiny blisters on the cornea, and occasionally a light cough, irritation of the nose and pharynx, and nausea. The most exposed developed conjunctivitis and blepharitis. Large variability between individual responses. | Is exposure to $H_2S$ reliable? No other gases were tested for. Workers in a similar tunnel, but with no $H_2S$ detected, had no eye irritations. Reasonable descriptive information (intermittent exposure of 50 people), relevant to $H_2S$, but the issue of repeated and intermittent exposure is not discussed. Are the same persons equally at risk, are some repeatedly more sensitive than others, etc.? | Larsen (1944) |

TABLE 3. STUDIES OF OCCUPATIONAL EXPOSURE TO $H_2S$ (pg. 2 of 4)

| Compound(s) Concentration(s) $mg/m^3$ (ppm) Duration | Population Group Description | Exposed | Controls | Effects | Remarks | Reference |
|---|---|---|---|---|---|---|
| $H_2S$ ~142 (~100) Apparently a one-time measurement for a problem which lasted several years. | Coal miners | 120 | — | Symptoms of eye irritation occurred after several hours of exposure. Wide variability in severity of response. The light cases exhibited burning, conjunctival congestion, and lacrimation; symptoms disappearing in several hours. Severe cases exhibited intense burning, gritty sensation, conjunctival congestion, photophobia, blepharospasm, abundant lacrimation, and violent headaches lasting up to a week. No habituation was found, and possible evidence of sensitization. | The one $H_2S$ measurement done used an imprecise method, so the value is doubtful. From the range of clinical symptoms, it is evident that considerable variation in exposure levels occurred, which are essentially not measured. Without dose/duration measurement, it is difficult to see the value of this descriptive report to this project. | Deveze (1956) |
| $H_2S$ 13.7-36.6 (10-26) | Workers in a sugar beet processing plant | Not given | — | Eye complaints were seen generally at the higher $H_2S$ levels: pains, light sensitivity, tears, and headaches. Problems lasted several hours to days, and some workers had repeated eye pain. | No controls or comparison group. Apparently no other gases or compounds tested for. | Kranenburg and Kessener (1925) |
| $H_2S$ 15-35 (levels measured 4.3 h after exposure) (11-25) | Accidental exposure of workers in a viscose plant while repairing a tank heater. | 9M | — | 4/9 complained of nausea, weakness, and pain in the chest, and were hospitalized. After 1 wk, no symptoms were found on internal, eye, neurological, and psychiatric examination and EKG. 5/9 were only briefly affected. All were examined 2 y later, and no after-effects were found. | | Prouza (1970) |

**TABLE 3. STUDIES OF OCCUPATIONAL EXPOSURE TO $H_2S$ (pg. 3 of 4)**

| Compound(s) Concentration(s) $mg/m^3$ (ppm) Duration | Population Group Description | Exposed | Controls | Effects | Remarks | Reference |
|---|---|---|---|---|---|---|
| $H_2S$ 28.4 (20) Daily exposure level often exceeding this | Shale oil plant workers. Controls from the shale quarry. | 459 M | 384 M | Frequency of nonoccupational disease the same in both groups. Plant workers reported 20% more fatigue, 5% more loss of appetite, and increased irritability. Slightly more headaches, loss of memory, and itching. 50% more complaints from conjunctivitis and 25% more from respiratory tract. Frequency of reported fatigue increased with length of employment and degree of exposure. | Attempt at non-concurrent prospective evaluation that falls down because of limited information on duration of exposure. Rates of symptoms are determined regardless of exposure duration and then stratified by those employed > or, < 2 y. Since dramatic differences are present between these two groups, it would have been imperative to calculate person-month or person-year exposure to determine accurately differences in symptom frequency. The marked difference in fatigue, greater in Group I (exposed to $H_2S$) with light work load, suggests possibility of (1) interviewer bias or (2) drift of less physically fit worker to Group I. These potential biases are not discussed. | Ahlborg (1951) |
| $H_2S$ 7.1-14.2 (5-10) $SO_2$ not given "lower aliphatic compounds." Probably for at least several years. | Gasoline desulfurization plant workers. | 20 | 20 workers of the same age from another dept. of the same plant. | There were 93 possible symptoms of irritation in exposed workers versus 23 for controls; 34 vs 7 respiratory; 20 vs 8, gastroenteritis; 30 vs 3, eye; and 9 vs 3, skin. | A survey of 40 workers in a petrol desulfurization plant, 20 of whom were at risk of toxicity to both $H_2S$ and $SO_2$. Comparability of the two groups is not determined. Data suggests that low-level exposure to 5-10 ppm may have respiratory and mucous membrane effects. Duration of exposure needs to be determined. | Benini and Colamussi (1969) |
| $H_2S$ 7.1-14.2 (5-10) $SO_2$ not given 5-15 y (at least one worker had only intermittent exposure). | Gasoline desulfurization plant workers. | 30 | — | Nine workers showed dermal affectations, 4 with papuloprurities and erythematous-wheal-like lesions (possibly indicating an allergic response), and 1 presented a syndrome of cutanea inveterata, pannicolopatia of the Besnier-Boek-Schaumann type and a miliary sarcoidosis of the lung of recent insurgence. Two of the above 5 were sensitive to solution of $H_2S$ in water as a patch test. | A descriptive survey of 30 workers, with no control or comparison group. | Benini and Colamussi (1969) |

TABLE 3. STUDIES OF OCCUPATIONAL EXPOSURE TO $H_2S$ (pg. 4 of 4)

| Compound(s) Concentration(s) $mg/m^3$ (ppm) Duration | Population Group Description | Exposed | Controls | Effects | Remarks | Reference |
|---|---|---|---|---|---|---|
| $H_2S$ <14.2 (<10) Actual measurements weren't made; an alarm set for this level never went off. | Workers in a heavy water plant. | Not given. | — | In 7 y, 123 cases of over-exposure were seen: weakness, nausea, dizziness, headache, and nervousness. Includes several reports of apparently higher exposures, resulting in more severe symptoms and unconsciousness. A perforated eardrum and alcohol consumption both seem to increase the toxicity of $H_2S$. | This is a descriptive uncontrolled study in which there is no correlation of duration of exposure (e.g. distance from source, length of employment) and subsequent symptoms. Largely anecdotal account of the relationship of alcohol and $H_2S$, and the problem with perforated eardrums. | Poda (1966) |

**TABLE 4. SUMMARY OF HUMAN EXPERIMENTAL EXPOSURE TO $H_2S$**

| $H_2S$ Level ($mg/m^3$) | (ppm) | Exposure | Effects | Reference |
|---|---|---|---|---|
| 0-7 | (0-5.0) | Acute | Minor coughing and burning throats in some subjects exposed to 2.5 and 5.0 ppm $H_2S$ for 15 minutes. No changes in blood chemistry or respiratory parameters. | Bhambhani and Singh (1985) |
| 0.20–0.96 | (0.009–0.7) | Acute | All people in the test group detected the odor. | Loginova (1957) |
| 0.08–0.50 | (0.06–0.36) | Acute | Range of odor thresholds within a group. | Baikov (1963) |
| 0.27 | (0.19) | Acute | Range of odor thresholds within a group. | Williams et al (1977) |
| 0.15 | (0.11) | Acute | Threshold of objectionability (not odor). | Tonzetich and Ng (1976) |
| 0.1 | (0.07) | Acute | Most people in the test group detected the odor. | Loginova (1957) |
| 0.031–0.09 | (0.02–0.06) | Acute | Some of the people in the test group detected the odor. | Loginova (1957) |
| 0.012–0.03 | (0.008–0.021) | Acute | Range of odor thresholds within a group. | Duan (1959) |
| 0.012–0.026 | (0.008–0.018) | Acute | Odor was not detected. | Loginova (1957) |
| 0.012–0.013 (2 studies) | (0.008–0.009) | Acute | Increased light sensitivity-related eye responses. | Baikov (1963) Duan (1959) |
| 0.010–0.013 (2 studies) | (0.007) | Acute | One study found significantly increased light sensitivity-related eye responses. The other study did not. | Duan (1959) Baikov (1963) |
| 0.005–0.009 | (0.004–0.006) | Acute | Range of "calculated" odor thresholds within several groups. | Adams et al (1968) |
| 0.008 | (0.006) | Acute | No effect on the ability of the eye to adapt to darkness. | Duan (1959) |
| 0.00067 | (0.0005) | Acute | Lowest concentration at which all subjects recognized the odor. | Leonardos et al (1969) |

TABLE 5. HUMAN EXPERIMENTAL EXPOSURE TO $H_2S$ (pg 1 of 2)

| Compound(s) Concentration(s) in mg/m$^3$ (ppm) | Mode of Exposure | No. of Test Subjects | No. of Controls | Duration and Frequency of Exposures | Total Length of Experiment | Effects | Reference |
|---|---|---|---|---|---|---|---|
| $H_2S$ 0-7 (0-5.0) | Mouth breathing | 42 (30 M, 12 F) | Subjects served as own control | 15 min. | 30 min. | No significant effects of $H_2S$ on hematogical variables, $PO_2$, $PCO_2$, $O_2$, content base excess or pH. | Bhambhani and Singh (1985) |
| $H_2S$ 0.012-0.96 (.009-.686) | Inhalation | 11, 16-55 y | Served as own controls | Exposures at each level repeated several times for unknown length of time | — | Odor not perceptible at 0.012-0.026 mg/$H_2S$/m$^3$. Varying odor perception at 0.031-0.090 mg/mm$^3$. Most perceived the odor at 0.10, and all did at 0.20-0.96 mg/m$^3$. Taking into account individual sensitivity authors give the odor threshold of $H_2S$ as 0.040 mg/m$^3$. | Loginova (1957) |
| $H_2S$ 0.08-0.5 (.057-.357) | Inhalation | 14, 18-30 y, "practically healthy" | — | Not given, 1 test/d, daily for 3-4 d | — | Range of odor thresholds. | Baikov (1963) |
| $H_2S$ 0.27 (0.19) | Olfactometer with sniffing tubes | 10 | — | Not given | — | Odor threshold. | Williams et al (1977) |
| $H_2S$ 0.15 (0.11) | Inhalation | 8, 20-30 y | — | Not given | — | Threshold of odor objectionability (not odor detection). | Tonzetich and Ng (1976) |
| $H_2S$ 0.012-0.030 (0.009-0.021) | Inhalation | 12 | — | 20-35 "observations" | — | Range of minimum concentrations at which the odor of $H_2S$ was smelled. | Duan (1959) |
| $H_2S$ 0.013 (0.009) | Inhalation | 3 | Served as own controls prior to exposure | 5 min., once during min. 15-20 of the expt. | 60 min. | Light sensitivity-related eye responses increased slightly more than at the 0.010 mg/m$^3$ exposure level, for the 40 min. following exposure. | Duan (1959) |

TABLE 5. HUMAN EXPERIMENTAL EXPOSURE TO $H_2S$ (pg 2 of 2)

| Compound(s) Concentration(s) in mg/m³ (ppm) | Mode of Exposure | No. of Test Subjects | No. of Controls | Duration and Frequency of Exposures | Total Length of Experiment | Effects | Reference |
|---|---|---|---|---|---|---|---|
| $H_2S$ 0.012 (0.009) | Inhalation | 3, 18-28 y | Served as own controls prior to exposure | 5 min. during min. 15-20 of a 60-min. expt., repeated on 3 days | 180 min. | Statistically significant increase in light sensitivity of the eye in the 40 min. following exposure. | Baikov (1963) |
| $H_2S$ 0.010 (0.007) | Inhalation | 3 | Served as own controls prior to exposure | 5 min., once, during min. 15-20 of the expt. | 60 min. | Statistically significant increase in the light sensitivity-related eye responses by the 20th min., and for the following 40 min. | Duan (1959) |
| $H_2S$ 0.010 (0.007) | Inhalation | 3, 18-28 y | Served as own controls prior to exposure | 5 min., during min. 15-20 of a 60-min. expt., repeated on 3 days | 180 min. | No effect on light sensitivity of the eye. | Baikov (1963) |
| $H_2S$ 0.005-0.009 (0.003-0.006) | Inhalation chamber with face exposure only | 998 M & F ~ 20 y | — | 15 s, once | — | Range of means of calculated odor thresholds from four test groups. | Adams et al (1968) |
| $H_2S$ 0.008 (0.006) | Inhalation | 3 | Served as own controls prior to exposure | 5 min. once, during min. 15-20 of the expt. | 60 min. | Ability of eye to adapt to darkness not affected. | Duan (1959) |
| $H_2S$ 0.00067 (0.00047) | Odor test room | 4 trained odor analysts | Served as own controls | — | — | Lowest concentration at which all the subjects positively recognized the odor. | Leonardos et al (1969) |

**TABLE 6. SUMMARY OF ACTUAL EXPOSURES TO $H_2S$ (pg. 1 of 2)**

| $H_2S$ Level ($mg/m^3$) | (ppm) | Time | Species | Effects |
|---|---|---|---|---|
| 130-150 | (93-107) | 7 h/d; 8 wk | DOG | Quiet, nausea, coughing, moderate conjunctival irritation, breathing difficulties at the end of each day. No significant blood changes. |
| 146.3 | (104) | 48 h | GPG | Forced breathing, some death, slow recovery of survivors. |
| 142 | (100) | ?/d; 15 d | RBT | Some initial eye irritation. Quiet, exhausted looking, slight decrease in respiratory frequency. |
| 142 | (100) | 30 min/d; 4 mo | RBT | No change in general condition. Some slight changes in blood parameters. |
| 142 | (100) | 7 d | RAT GPG | No histopathologic lesions or clinicopathologic changes. |
| 71-142 | (50-100) | 4 d | GOAT | Increased rectal temperature, decreased food and water intake, and increased plasma cortisol levels. All returned to normal by the end. |
| 41.6–142 | (30-100) | 8-24 h | MUS | Hypothermia, decreased food and water intake, weight loss, ~50% mortality. Pathological changes in the major organs. Survivors recovered their weight in ~2 wk. |
| 50-100 | (35-70) | 5 d | RBT | No eye lesions. |
| 49.7–92.3 | (35-65) | 16 h | RAT | Lethargy and heavy breathing by the end. Extensive organ damage in the one that died. |
| | | 100 h | RAT | Eye and nose irritation, rough hair. Recovered. |
| | | 100 h | GPG | Nose and eye irritation, rough hair. Recovered. |
| 50 | (35) | 6 h/d; 6 mo | RAT | Decreased $O_2$ consumption. Increased erythrocyte and active neutrophil content, permeability of vessels, and respiration in heart and lung tissue. |
| 142–42/6 | (10-30) | ?/d; 20 d | RBT | No change in respiration rate, WBC, RBC, hemoglobin, and autopsy findings. Slight weight decrease. |
| 28.4 | (20) | 48 h | MUS | Decreased food and water intake and rectal temperature. Weight loss. |
| 28.4 | (20) | 90 d | MUS | Some mortality, survivors showing brain, liver, and lung abscesses. Survivors lost weight, had less endurance, and had instances of broncho-pneumonia and hepatitis. |
| 28.4 | (20) | 90 d | RAT | 24% mortality, weight loss, lung pathology, and significant changes in many blood parameters. |
| 28.4 | (20) | 1 h/d 11 d | GPG | Fatigue, somnolence, dizziness, itching, and eye irritation. Decreased lipids in cerebral hemisphere and brain stem. |
| 28.4 | (20) | 90 d | MKY | Weight loss. Changes in many blood parameters. |
| 28.4 | (20) | 21 d | COW | No effect of feed intake, milk production, or heart rate. Slight lacrimation. |

GPG = Guinea pig
CAN = Canary
RBT = Rabbit
MKY = Monkey
MUS = Mouse

**TABLE 6. SUMMARY OF ACTUAL EXPOSURES TO $H_2S$ (pg. 2 of 2)**

| $H_2S$ Level ($mg/m^3$) | (ppm) | Time | Species | Effects |
|---|---|---|---|---|
| 22.7 | (15) | 16 h<br>16 h | MUS<br>RAT | Slight restlessness. Normal autopsy. Slight initial restlessness. |
| 14.2 | (10) | 5 d | MUS | Initial decrease in temperature. Decreased food and water intake, with some recovery by the end. |
| 14.2 | (10) | 41 d | RAT | Also under cold stress, and showed decreased weight gain and food utilization. No changes in blood cells, plasma protein, or weight of liver and lungs. |
| 14.2 | (10) | 4 d | GOAT | Initial decrease in food and water intake. |
| 14 | (10) | 7 h/d;<br>14 d | DOG | Some coughing. Increased water consumption after each exposure. No change in blood picture or body weight. |
| 12.1 | (9) | 17 d | PIG | NOEL for body weight gain and respiratory system. |
| 10 | (7) | 3 h/d;<br>3 mo | RAT | Weight gain retarded. Changes in motor chronaxie. Irritation of mucous membranes of trachea and bronchi. |
| 10 | (7) | 6 h/d;<br>4 mo | RAT | Retarded weight gain. Changes in some blood parameters (increased hemoglobin). $O_2$ consumption decreased by the end. Changes in lung and heart enzyme activity. |
| 4.86–9.36 | (4-7) | 6 h/d;<br>4 mo | RAT | Decreased liver glycogen and lipid levels; blood sugar, and erythrocytes. Increased blood lipids, hemoglobin, and leukocytes. |
| 0.02 | (0.01) | 12 h/d;<br>3 mo | RAT | Changes in motor chronaxie. No change in weight. No pathological changes found in sacrificed animals. |

TABLE 7. BIOASSAYS ON $H_2S$ EFFECTS (pg. 1 of 2)

| Compound and Concentration in mg/m³ (ppm) | Temperature and Humidity | Preparation Exposed | Description of Tests and Duration | Results | Reference |
|---|---|---|---|---|---|
| $H_2S$ 153.4 (108) | | Rat (albino, ITRC colony) lung homogenate | ≤5 ml of $H_2S$ gas was injected from a glass syringe into a pre-evacuated glass vial containing 5 ml of the homogenate. The exposed supernatant was kept in the cold for 1 h, then enzyme levels were measured. | Inhibited:<br>Acid phosphatase 38.5%<br>Alkaline phosphatase 35.0%<br>GPT 38.2%<br>GOT 16.5%<br>ATPase 32.0%<br>Stimulated: arginase<br>No effect: aldolase | Husain (1976)<br>Husain and Zaidi (1977) |
| $H_2S$ 85.2 (60) | | Alveolar macrophages obtained by lavage of the lungs of male New Zealand White rabbits | Cell cultures were exposed to $H_2S$ for 24 or 48 h in the airstream of a flow-through incubator. Those exposed for 24 h were then given 24 h recovery time. Phagocytic ability was measured at 48 h. Two types of culture methods were used. | Only exposure for 48 h (no recovery time) had an effect on phagocytic ability (~20% decrease) of cells cultured on gas-impermeable flasks. Cells cultured on gas-permeable membranes (more similar to in vivo exposure) showed ~95% inhibition of phagocytic ability after 24 h exposure with 24 h recovery and after 48 h exposure. | Robinson (1980) |
| $H_2S$ av. 76.5 (avg. 53.9) | | Alveolar macrophages obtained by lavage of the lungs of male New Zealand White rabbits | Cell cultures were exposed to $H_2S$ in the airstream of a flow-through incubator for one of several different regimens: 8 h; 8 h + 16 h delay + 8 h; 8 h + 16 h delay + 8 h + 16 h; or 24 h. Phagocytic ability was measured 24 h after the last exposure (presumably of each regimen). | Exposure for 8 h had no effect on phagocytic ability. Intermittent exposures caused a definite decrease and continuous exposure caused even greater reductions (0-11% of the controls). | Robinson (1980) |
| $H_2S$ 71 (50) | | Alveolar macrophages obtained by lavage from the lungs of New Zealand White rabbits of either sex | Cell cultures were exposed to $H_2S$ for 20 h in the airstream of a flow-through incubator. After 24 h recovery, phagocytic ability and viability of the cells were determined. | Relative to controls:<br>Phagocytic ability 88%<br>Viability 88-94% | Robinson (1979) |

**TABLE 7. BIOASSAYS ON $H_2S$ EFFECTS (pg. 2 of 2)**

| Compound and Concentration in mg/m³ (ppm) | Temperature and Humidity | Preparation Exposed | Description of Tests and Duration | Results | | Reference |
|---|---|---|---|---|---|---|
| $H_2S$ 56.8 (45.6) | | Rat (albino, ITRC colony) lung homogenate | ≤5 ml of $H_2S$ gas was injected from a glass syringe into a pre-evacuated glass vial containing 5 ml of the homogenate. The exposed supernatant was kept in the cold for 1 h, then enzyme levels were measured. | Inhibited:<br>Acid phosphatase<br>Alkaline phosphatase<br>GPT<br>GOT<br>ATPase<br>Stimulated: arginase<br>No effect: aldoase | <br>33.0%<br>19.5%<br>27.9%<br>19.5%<br>24.0%<br>23.8% | Husain (1976)<br>Husain and Zaidi (1977) |
| $H_2S$ 25.8 (18.2) | | Rat (albino, ITRC colony) lung homogenate | ≤5 ml of $H_2S$ gas was injected from a glass syringe into a pre-evacuated glass vial containing 5 ml of the homogenate. The exposed supernatant was kept in the cold for 1 h, then enzyme levels were measured. | Inhibited:<br>Acid phosphatase<br>Alkaline phosphatase<br>GPT<br>GOT<br>ATPase<br>Stimulated: arginase<br>No effect: aldolase | <br>16.8%<br>11.0%<br>25.9%<br>15.9%<br>13.3%<br>22.0% | Husain (1976)<br>Husain and Zaidi (1977) |

TABLE 8. CANARIES — ACUTE EXPERIMENTAL EXPOSURE TO $H_2S$

| Compound(s) and Concentration(s) in mg/m³ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 99.4-142 (70-100) | Not given | Exposure chamber | Canaries | 6 | None | 8 h, once | 44 h | Between 30 min and 1 h, one case of slight edema and one case of panting were recorded. At 1-4 h, edema, dizziness, general stupidity, and forced breathing through the mouth were noted. From 4-8 h, very forced respiration, edema, dizziness, unconsciousness, and death occurred. Those surviving the actual exposure died in the following 12-36 h. | Mitchell and Yant (1925) |
| $H_2S$ 49.7-92.3 (35-65) | Not given | Exposure chamber | Canaries | 2 | None | 18 h, once | | At 4-8 h, stupid, heavy breathing, edema. At 8-18 h, weakness — inability to perch; death. | Mitchell and Yant (1925) |

**TABLE 9. MICE — ACUTE EXPERIMENTAL EXPOSURE TO $H_2S$ (pg. 1 of 2)**

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 142 (110) | 25°C | Inhalation chamber | Mice Swiss Webster | 8 F | 8 controls treated same, 8 mice deprived of food and water (controls accidentally exposed to 20–30 ppm; see 30 ppm entry) | 8 h once | 8 h | Modified lethal concentration duration 50 was 7.5 h. Three mice died and rest were hypothermic. Erythrocyte carbonic anhydrase activity (an enzyme involved in the handling of $CO_2$, and so reflects the non-oxygen side of respiration) not inhibited. Mice did not eat or drink available food or water. | Hays (1972) |
| $H_2S$ 89.5 (63) | 74.6 + 8.8% 73.3 + 3.3% | Continuous flow inhalation chamber | Mice | 4 | None | 16 h, once | 16 h | 50% mortality after 804 min. One survived the test but died 23 h later.<br>Animals were found to have congested brains, massive lung hemorrhages, pale and enlarged livers, distended stomachs with few moderate-sized hemorrhages, and pale kidneys. | Weedon et al (1940) |

TABLE 9. MICE — ACUTE EXPERIMENTAL EXPOSURE TO $H_2S$ (pg. 2 of 2)

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 71 (50) | 25°C | Inhalation chamber | Mice Swiss Webster | 8 F | 8 controls treated same, 8 deprived of food and water (Controls accidentally exposed to 20–30 ppm; see 30 ppm entry) | 16 h, once | 16 h | Modified lethal concentration duration 50 was 15 h. Animals were hypothermic. Erythrocyte carbonic anhydrase activity not inhibited. Food and water intake reduced 70% during exposure. | Hays (1972) |
| $H_2S$ 41.6 (30) | 25°C | Inhalation | Mice | 8 F | 8 controls treated the same, and 8 mice deprived of food and water (Both groups accidentally exposed to 20–30 ppm $H_2S$) | 24 h, once | 13 d | The modified lethal concentration duration 50 was 18.5 h. Three mice died and the rest were hypothermic. Two mice died at 42 h. By day 4 rectal temperatures had increased to pre-exposure level. Food and water intake decreased and mice lost weight. By day 13 weight had returned to normal. | Hays (1972) |
| $H_2S$ 22.7 (16) | 74.6 + 8.8% 73.3 + 3.3% | Continuous flow inhalation chamber | Mice | 4 | None | 16 h, once | 16 h | No abnormal reactions other than an initial slight restlessness which quickly disappeared. Autopsy normal. | Weedon et al (1940) |

**TABLE 10. MICE — REPEASED DOSE EXPERIMENTAL EXPOSURE TO $H_2S$**

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 142 (100) | 25°C | Inhalation | Mice NMRI | 20 F | 8 F | 2 h every 4 d; 1-4 times | 2-8 hr | No effect on cerebral protein content. Decreased RNA and orotic acid uptake. Decreased lysosomal acid proteinase activity. Transient ↑ glutathiene cont. after second exposure.↑ superoxide dismutase activity only after first exposure. Cumulative inhibition of cyt. $aa_3$ but no change in ACLE activity ↑ 2',3' — cyclic nucleotide 3' — phosphohydrolase activity. Excitement of mice during initial part of exposure period. No deaths or clinical signs of $H_2S$ intoxication. | Savolainen et al (1980) |
| $H_2S$ 28.4 (20) | 25°C | Inhalation chamber | Mice Swiss Webster | 7M | 7 controls treated same, 7 mice deprived of food and water | 48 h, once | 48 h | Food and water intake decreased 20%, rectal temperatures decreased 3.7°C, and animals lost weight. Sleep time as induced by pentobartibal not different from control except deprived group slept longer. | Hays (1972) |
| $H_2S$ 14.2 (10) | 25°C | Inhalation chamber | Mice Swiss Webster | 6 F | 6 F | 5 d, once | 5 d | No deaths. Body temperature dropped significantly after 48 h exposure but was not significantly different from controls during rest of study. Erythrocyte carbonic anhydrase activity not inhibited. Food and water intake dropped 60% during first 24 h but was inhibited only 28% by day 5 as compared to controls. | Hays (1972) |

TABLE 11. MICE — CHRONIC EXPERIMENTAL EXPOSURE TO $H_2S$ (pg. 1 of 2)

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 28.4 (20) | 50 ± 10% 70 ± 5°F (Control room up to 86°F) | Exposure chamber | Mice, avg. wt. 25 g | 100 M | 100 M | 90 d, continuous | 90 d | Mortality 26% versus 16% in controls. Statistically significant weight loss after 90 d and decrease in swimming endurance compared to controls. Lung pathology present in 33% of animals autopsied compared to 17% in controls.<br>Statistically significant changes in blood parameters at 90-d exposure over pre-exposure levels; leukocytes, hematocrit, hemoglobin. MCV, MCHb, increased; erthrocytes decreased. Compared with controls at 90 d: leukocytes, reticulocytes, hematocrit, hemoglobin, MCV (mean corpuscular volume), MCHb (mean corpuscular hemoglobin), increased; platelets decreased.<br>Mice that died during test period exhibited abcesses of the brain, liver, and lung. Sacrificed animals exhibited instances of broncho-pneumonia and hepatitis. | Sandage (1961) |

**TABLE 11. MICE — CHRONIC EXPERIMENTAL EXPOSURE TO $H_2S$ (pg. 2 of 2)**

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 28.4, 42.7, 112, (10, 30, 80) | 25-77% 61-80°F | Inhalation chamber | Mice $B_6C_3F_1$ | 40 M<br>48 F | 10M<br>12 F | 90 d,<br>6 h/d,<br>5 d/wk | 90 d | Biologically significant depression of body weight gain at 80 ppm. A few significant differences in food consumption. No eye abnormalities. Neurologically, eye of 1 mouse each at 30 and 80 ppm did not respond to artificial light stimulus. No significant differences in hematology, serum chemistry or urinalysis data. No gross pathology changes. Histopathology showed 89% males and 78% of females at 80 ppm had inflamed nasal mucosa in anterior nose. | CIIT (1983) |

TABLE 12. RATS — ACUTE EXPERIMENTAL EXPOSURE TO $H_2S$

| Compound(s) and Concentration(s) in mg/m³ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 89.5 (63) | 74.6 ± 8.8% 73.3 ± 3.3°F | Continuous flow inhalation chamber | Rats | 8 | None | 16 h, once | 16 h | 50% mortality not reached. Animals unaffected at first but by 16 h they were lethargic and breathing heavily. One rat died, and it had congested brain, half of lung collapsed, moderately dark red liver and kidneys, distended stomach and caecum. | Weedon et al (1940) |
| $H_2S$ 22.7 (16) | 74.6 ± 8.8% 73.3 ± 3.3°F | Continuous flow inhalation chamber | Rats | 8 | None | 16 h, once | 16 h | No abnormal reactions other than a slight initial restlessness. | Weedon et al (1940) |

**TABLE 13. RATS — REPEATED DOSE EXPERIMENTAL EXPOSURE TO $H_2S$ (pg. 1 of 3)**

| Compound(s) and Concentration(s) in mg/m³ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 142-198.8 (100-140) | Not given | Exposure chamber | Rats | 19 | Not given | ≤48 h, once | — | 1-4 h: indication of irritation to the nose by continual washing of face. 4-8 h: irritation of nose and eyes. 8-18 h: forced breathing. 18-48 h: death or very slow recovery following exposure. | Mitchell and Yant (1925) |
| $H_2S$ 142 (100) | Not given | Inhalation | Rats | Not given | Not given | 7 d | 7 d | No significant histopathologic lesions or clinicopathologic alterations. | Renne and McDonald (1979) |
| $H_2S$ 142 (100) | Not given | Inhalation | Rats | Not given | Not given | 7 d | 7 d | No significant histopathologic lesions or clinicopathologic alterations. | Renne and McDonald (1979) |
| $H_2S$ 49.7-92.3 (35-65) | Not given | Exposure chamber | Rats | 4 | Not given | 100 h, continuous | 100 h | 1-4 h: showed irritation to nose by continued washing of face. 4-8 h: irritation of nose and eyes. 8-18 h: quiet. 18-48 h: pus in eyes and nose, hair rough. No worse after 100 h continuous exposure. | Mitchell and Yant (1925) |
| $H_2S$ 28.4 (20) | 50 ± 10% 75 ± 5°F (Control room up to 86°F) | Inhalation | Rats, Sprague-Dawley, general purpose strain, avg. wt. 175 g | 50 M | 50 M | 90 d, continuous | 90 d | Mortality 24% versus 4% in controls. Significant weight loss after 90 d. Lung pathology present in 33% and kidney pathology in 6% of animals autopsied. Statistically significant changes in blood parameters at 90 d exposure over pre-exposure levels: platelets, reticulocytes, hematocrit, hemoglobin, MCV, MCHb, increased. Compared with controls in 90 d: leukocytes and reticulocytes, increased; platelets, decreased. | Sandage (1961) |

TABLE 13. RATS — REPEATED DOSE EXPERIMENTAL EXPOSURE TO $H_2S$ (pg. 2 of 3)

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 14.2 (10) | 50-70% 10°C | Inhalation | Rats | 13 | 15 (2 control groups, one held under optimal temperature, other at 10°C) | 41 d | 41 d | After 7 wk, significantly less wt. gain, 81% for the test group versus 92% for controls under cold conditions both compared to controls at an optimal temperature. Food utilization reduced, 132% versus 122% for controls under cold conditions. No differences in blood cells, plasma protein, or wt. of liver and lungs. | Stolpe et al (1976) |
| $H_2S$ 14.2 (10) $NH_3$ 71 (50) | 50-70% 10°C | Inhalation | Rats | 12 | 20 (2 control groups, one held under optimal temperature, other at 10°C) | 50 d | 50 d | Significantly less wt. gain, 81% versus 92% for controls under cold condition. Food utilization reduced, 148% versus 122% for controls under cold conditions. No differences in blood cells, plasma protein, or wt. of liver and lungs. | Stolpe et al (1976) |
| $H_2S$ 7.1 (5) $NH_3$ 42.6 (30) | 50-70% 10°C | Inhalation | Rats | 12 | 13 (2 control groups, one held at optimal temperature, one at 10°C) | Continuous | 53 d | No differences in wt. gain from the cold control, both 92% of rats at optimal temperature. Food utilization reduced, 148% versus 122% for cold conditions. No differences in blood cells, plasma protein, or wt. of liver and lungs. | Stolpe et al (1976) |

**TABLE 13. RATS — REPEATED DOSE EXPERIMENTAL EXPOSURE TO $H_2S$ (pg. 3 of 3)**

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 28.4, 42.7 112 (10, 30, 80) | 25-77% 61-81°F | Inhalation | Rats F 344 | 15M 15 F | 15M 15 F | 6 h/d, 5 d/wk for 90 d | 90 d | No mortality. Clinically observed crustiness with ear tags, crusty nose, eye, muzzle; lacrimation, rales, yellow-brown fur, red-stained fur. Significant ↓ body weight gains in all groups of both sexes after first week of exposure. No effects with respect to food consumption, neurological function, clinical pathology and organ weight data. No gross or histopathological abnormalities. | CIIT (1983) |
| $H_2S$ 28.4, 42.7 112 (10, 30, 80) | 25-77% 61-81°F | Inhalation | Rats Sprague-Dawley | 15M 15 F | 15M 15 F | 6 h/d 5 d/wk for 90 d | 90 d | Same as for F 344 rats with exception that irritability, swollen muzzle and/or eye reported as well. Decreased brain weight in 80 ppm females. | CIIT (1983) |
| $H_2S$ 7.1 (5) $NH_3$ 42.6 (30) Dust 42.34 + 14.07 | 50-70% 10°C | Inhalation | Rats | 15 | 15 (2 control groups, one held under optimal temperature, other at 10°C, both exposed to dust same as test rats) | 44 d, exposed to dust for 1 h, 2 times/d, 5 d/wk | 44 d | Less wt. gain than cold controls, 87% versus 92%. Food utilization reduced, 130% versus 122% for controls under cold conditions.<br><br>No differences in blood cells, plasma protein, or wt. of liver and lungs. | Stolpe et al (1976) |

TABLE 14. RATS — CHRONIC EXPERIMENTAL EXPOSURE TO $H_2S$ (pg. 1 of 3)

| Compound(s) and Concentration(s) in mg/m³ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 50<br>CO 300 | Not given | Inhalation chamber | Rats albino | Not given | Not given | 4 h/d, 6mo | 6mo | $O_2$ consumption lowered 17%. Erythrocyte content increased 11%, Hb content not significantly changed.<br><br>Summation: threshold index down 83% at 2 wk (controls down 93%) but later increased to 120% of original value (controls were 104% of original value).<br><br>Increased respiration in heart and lung tissue, no change in kidneys. Significant increase in percent of active neutrophils. Increased permeability of vessels. | Melnichenko (1968) |
| $H_2S$ 10 | Not given | Inhalation chamber | Rats, albino 60-90 g | 10M | 10M | 12 h/d, "except days off," for 3 mo | 17 wk | Wt. retarded compared to controls. Changes in the motor chronaxie (a measure of nerve cell function) of rats. In controls chronaxie of a straightening is consistently above the chronaxie of flexing. After 2 wk exposure the two reversed and remained that way through 6 wk; over the next 3 wk the two returned to normal positions, reversed again, and finally moved back toward a normal relationship.<br><br>In the 2 rats killed for study, there was a slight irritation of mucous membranes of trachea and bronchi. Changes in appearance of some dendrites in brain cortex. | Duan (1950) |

TABLE 14. RATS — CHRONIC EXPERIMENTAL EXPOSURE TO $H_2S$ (pg. 2 of 3)

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 10 (7) (Concentration reported as MAC, no value given. This value taken from 1972 MAC in U.S.S.R., 1972) | Not given | Inhalation chamber | Rats, albino | 26 | 26 | 6 h/d | 4 mo | Retardation of wt. gain. No significant changes in number of erythrocytes. Hb content of blood significantly increased. Number of leukocytes fluctuated up and down over 4 mo, was higher than controls at end. $O_2$ consumption increased slightly at beginning, then decreased to 21.4% less than controls. No significant change in succinate dehydrogenase (SDG) activity in lungs or kidneys. 16.7% decrease of SDG activity in heart. Activity of cytochrome oxidase in lungs increased 19.0%. | Aitbaev et al (1976) |
| $H_2S$ 9.35 + 0.51 (6.7) | Not given | Inhalation chamber | Rats, white, 80-200 g | 24 | 14 | 6 h/d, daily except Sunday, 4 mo | 4 mo | Reduced level of glycogen in liver (91.9%), lower blood sugar (69.1%), increased lipids in blood (202.6%), and lower lipids in liver (27.9%). Expressed lipemia present. Lowering of erythrocytes, significant increase of hemoglobin and leukocytes, and slight leukocytosis. | Elebekova et al (1976) |

TABLE 14. RATS — CHRONIC EXPERIMENTAL EXPOSURE TO $H_2S$ (pg. 3 of 3)

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 4.86 + 0.08 (3.5) | Not given | Inhalation chamber | Rats, white, 80-200 g | 22 | 14 | 6 h/d, daily except Sunday, 4 mo | 4 mo | Reduced level of glycogen in liver (68%), lower blood sugar (50.2%), lower lipids in liver (38.8%), and increased lipids in blood (98.6%). Expressed lipemia present. Increase in erythrocytes, hemoglobin, slight increase in eosinophils and segmented neutrophils, slight reticulocytosis, and sharp lowering of monocytes and lymphocytes. | |
| $H_2S$ 0.02 (0.01) | Not given | Inhalation chamber | Rats, albino, 60-90 g | 10M | 10M | 12 h/d, "except days off," for 3 mo | 17 wk | No change in wt. compared to controls.<br><br>Change in the motor chronaxie of rats. In controls chronaxie of straightening is consistently above the chronaxie of flexing. After 2 wk exposure the two were converging and stayed near the same through 7 wk. During the 7th wk chronaxie of flexing exceeded chronaxie of straightening, then the two moved back toward normal.<br><br>No pathological changes noted in 2 of the rats killed and examined. | Duan (1959) |

**TABLE 15. GUINEA PIGS — REPEATED DOSE EXPERIMENTAL EXPOSURE TO $H_2S$**

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 146.3 (103) | Not given | Exposure chamber | Guinea pigs | 2 | Not given | ≤48 h, once | — | 8-18 h: labored and forced breathing. 18-48 h: death in one case with slow recovery for the other. | Mitchell and Yant (1925) |
| $H_2S$ 142 (100) | Not given | Inhalation | Guinea pigs | Not given | Not given | 7 d | 7 d | No significant histopathologic lesions or clinicopathologic alterations | Renne and McDonald (1979) |
| $H_2S$ 142 and $NH_3$ 180 (250) | Not given | Inhalation | Guinea pigs | Not given | Not given | 7 d | 7 d | No significant histopathologic lesions or clinicopathologic alterations. | Renne and McDonald (1979) |
| $H_2S$ 49.7-92.3 (35-65) | Not given | Exposure chamber | Guinea pigs | 2 | Not given | ≤100 h, once | — | 8-18 h: hair rough. 18-48 h: hair rough, pus in eyes and nostrils, cough. No worse after 100 h continued exposure; all recovered. | Mitchell and Yant (1925) |
| $H_2S$ 28.4 (20) | 40% 30 ± 4°C | Inhalation chamber | Guinea pigs, 400--500 g | 6M | 6M | 1 h/d, 11 d | 11 d | Fatigue, somnolence, dizziness, itching, and eye irritation were observed. Significant lowering of total lipids and phospholipids in the cerebral hemisphere and brain stem, but no change in the levels in the cerebellum. No change in cholesterol level in any of these regions. Increased lipid peroxidation in the cerebral hemisphere. | |

TABLE 16. RABBITS — REPEATED DOSE EXPERIMENTAL EXPOSURE TO $H_2S$

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 142 (100) | | Inhalation chamber | Rabbits | 3M | None | ?/d ?/wk 15 d | 15 d | Temporarily increased eye secretion. Quiet, moderately exhausted-looking at the end. Slight decrease in respiratory frequency at the end of expt. No weight loss. 2/3 showed, on autopsy and microscopic examination, evidence of increased blood circulation in the gastrointestinal tract (including hyperemia and loss of the villus epithelium in the small intestine). | Weise (1933) |
| $H_2S$ 50-100 (35.2-70.4) | 90% 20°C | Inhalation chamber | Albino rabbits 1.5-2.0 kg | Not given | Not given | 5 d | 5 d | No evidence of any eye lesions was seen. | Masure (1950) |
| $H_2S$ 14.2-42.6 (10-30) | | Inhalation chamber | Rabbits | 2M | None | ?/d, ?/wk, 20 d | 20 d | No effect on respiration rate, white and red blood cell counts, hemoglobin levels, or appetite. Slight weight decrease. On autopsy, no changes. Some changes in microscopic exam. of the small intestine of one animal. | Weise (1933) |
| $H_2S$ 100 (71) | | Inhalation chamber | Rabbits 2.3-2.8 kg | 37 | 10 | Once for 1.5 h and 0.5 hr/d for 5 d | 1.5 h 5 d | Unconsciousness. Disorders or repolarization. No arrhythmias. In 5 d exposed animals observed arrhythmias that persisted several days post-exposure. Decreased ATP phosphorylase and $NADPH_3$ oxidoreductase in sarcolemma of muscle fibers and vascular endothelium. | Kosmider et al (1967) |

TABLE 17. RABBITS — CHRONIC EXPERIMENTAL EXPOSURE TO $H_2S$

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 142 (100) | Not given | Inhalation chamber | Rabbits domestic avg. wt. 20 kg | 4 | 4 | 30 min/d daily, 4 mo | 4 mo | No measurable abnormal findings in the general condition, body weight, number of erythocytes, serum calcium total serum protein, and serum protein fraction. There was decline in specific gravity of blood. Some slight changes such as oligochromenia, reticulocytosis, leucopenia, and relative lymphocytosis, which quickly returned to normal after exposure stopped. | Wakatsuki (1959) |
| $H_2S$ 28.4-35.5 (20-25) | Not given | Inhalation chamber | Rabbits, domestic, avg. wt. 20 kg | 5M | 5M | 4 h/d, 150 d | 210 d | No change in general state and specific gravity of blood. There was an initial increase in free cholesterol and fall in ester ratio that returned to normal levels after a short period. | Kuwai (1960) |

TABLE 18. MONKEYS — CHRONIC EXPERIMENTAL EXPOSURE TO $H_2S$

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 28.4 (20) | 50 ± 10% 57 ± 5°F (Control room up to 86°F) | Inhalation chamber | Rhesus monkeys, avg. wt. 1.7 kg | 10M | 10M | 90 d | 90 d | No death. Statistically significant weight loss after 90 d.<br><br>Statistically significant changes in blood parameters at 90 d exposure over pre-exposure levels: erythrocytes and amylase increased, and MCHb and MCHbC (mean corpuscular hemoglobin concentration) decreased. Compared with controls at 90 d: MCHbC decreased, and urine alkaline phosphatase increased. | Sandage (1961) |
| $H_2S$ 146.3 (103) | Not given | Exposure chamber | Dogs | 2 | Not given | ≤16 h, once | — | 4-8 h: lacrimination and depression. 8-16 h: pus in eyes, death. | Mitchell and Yant (1925) |

**TABLE 19. PIGS — REPEATED DOSE EXPERIMENTAL EXPOSURE TO $H_2S$**

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 12.1 (8.5) | 17–19°C | Inhalation chamber | Pigs cross-bred 13.2 kg | 3 (All of the same sex, unspecified) | 3 | 17 d | — | No effect on body wt. gain. No pathological changes in respiratory system. | Curtis et al (1975) |
| $H_2S$ 2.84 (2) $NH_3$ 36 (50) | 17–19°C | Inhalation chamber | Pigs cross-bred 13.2 kg | 3 (All of the same sex, unspecified) | 3 | 19 d | — | No effect on body wt. gain. No pathological changes in respiratory system. | Curtis et al (1975) |

TABLE 20. GOATS — REPEATED DOSE EXPERIMENTAL EXPOSURE TO $H_2S$

| Compound(s) and Concentration(s) in mg/m³ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 142 (100) | 17°C | Inhalation chamber | Goats, mixed breed, 3-4 y, 35-75 kg | 6 F | Served as own controls | 4 d, continuous | 4 d | Respiration frequency decreased, rectal temperature increased 0.7°C, returning to near normal after 4 d. Food and water intake decreased 37 and 25%, respectively, during first 2 d, regaining near normal levels after 4 d. Plasma cortisol increased but returned to normal levels after 4 d of exposure. | Hays (1972) |
| $H_2S$ 71 (50) | 17°C | Inhalation chamber | Goats, mixed breed, 3-4 y, 35-75 kg | 4 F | Served as own controls | 4 d, continuous | 4 d | Plasma cortisol increased (possibly indicating stress) and rectal temperature increased 0.7°C, but both returned to near normal after 4 d of exposure. Food and water intake decreased by 64% during the 2nd d, but increased some after 4 d. | Hays (1972) |
| $H_2S$ 14.2 (10) | 17°C | Inhalation chamber | Goats, mixed breed, 3-4 y, 35-75 kg | 4 F | Served as own controls | 4 d, continuous | 4 d | Food and water intake decreased by 20 and 63% respectively on first day, but returned to near normal levels thereafter. | Hays (1972) |

**TABLE 21. COWS — REPEATED DOSE EXPERIMENTAL EXPOSURE TO $H_2S$**

| Compound(s) and Concentration(s) in $mg/m^3$ (ppm) | Humidity and Temperature | Mode of Exposure | Species Strain Age/Weight | No. of Test Animals | No. of Controls | Duration and Frequency of Exposure | Total Length of Expt. | Effects | Reference |
|---|---|---|---|---|---|---|---|---|---|
| $H_2S$ 28.4 (100) | 50%, 20°C | Inhalation through exposure hood over cow's head | Cows (lactating), Holstein, avg. wt. 499 kg | 3 | Served as own controls prior to exposure | 21 d, continuous | 21 d | No effect on feed intake, milk production, or heart rate. Slight lacrimation. | Hays (1972) |

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